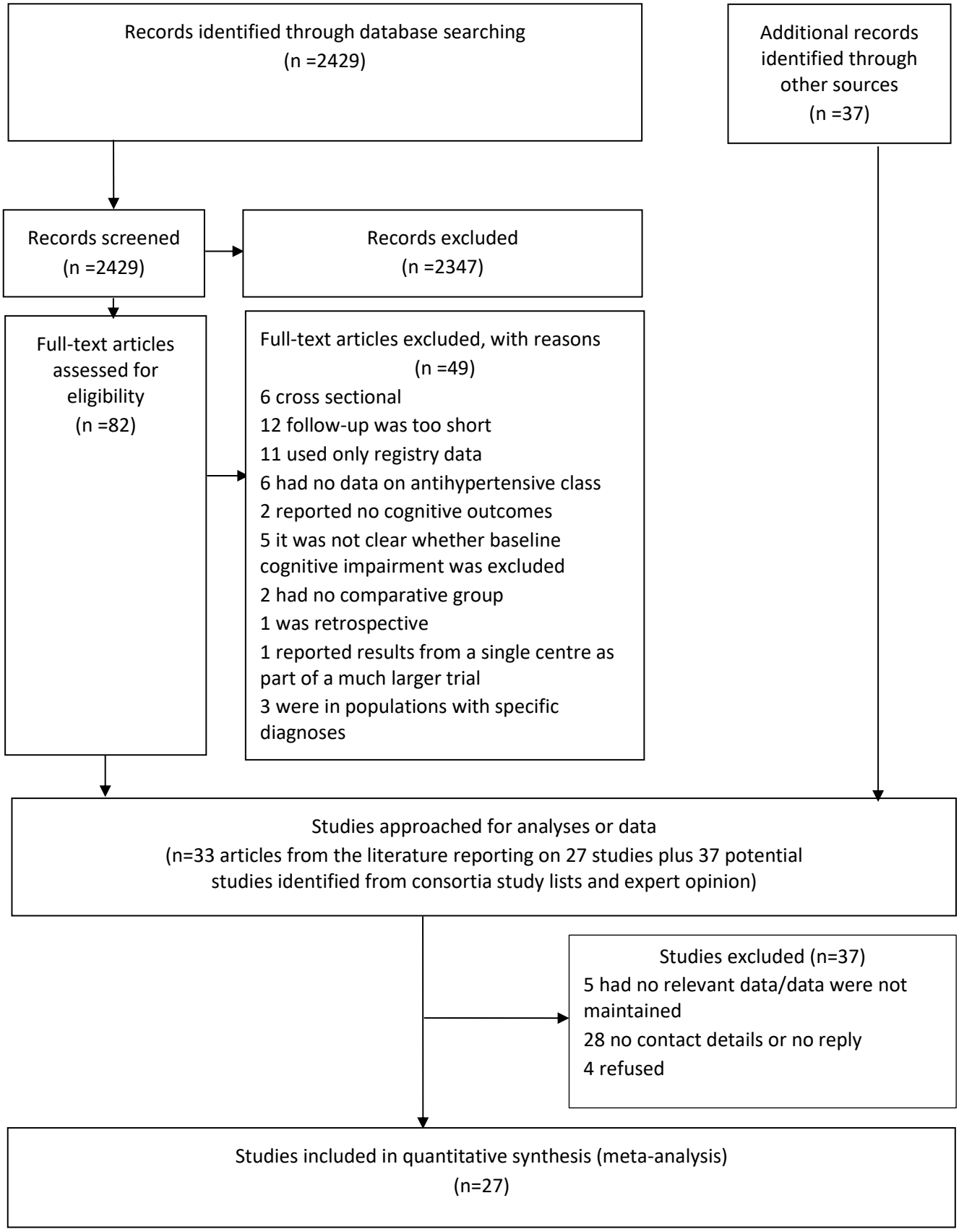
Peters, R., Yasar, S., Anderson, C., Andrews , S., Antikainen, R., Beckett, N., Beer, J. C., Bertens, A. S., Booth, A., van Boxtel, M., Brayne, C. E. G., Brodaty, H., Carlson, M. C., Chalmers, J., Corrada, M., DeKosky, S., Derby, C., Dixon, R. A., Forette, F., ... Anstey, K. J. (2019). An investigation of antihypertensive class, dementia and cognitive decline. A meta-analysis. *Neurology*. https://doi.org/10.1212/WNL.0000000000008732

Online only appendices

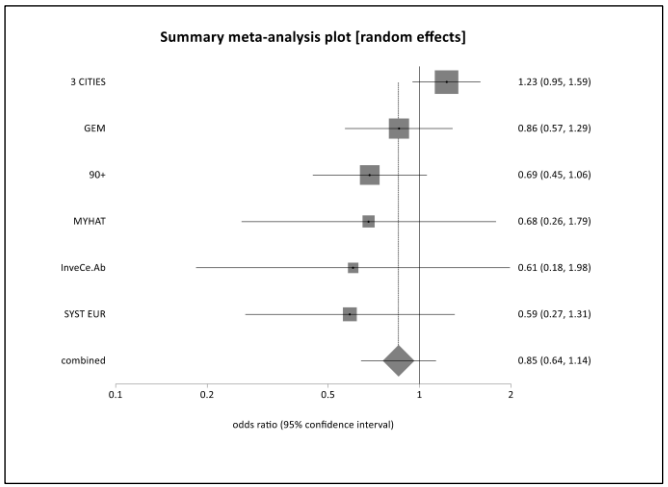
Study appendices

appendix-figure 1. Study flow chart

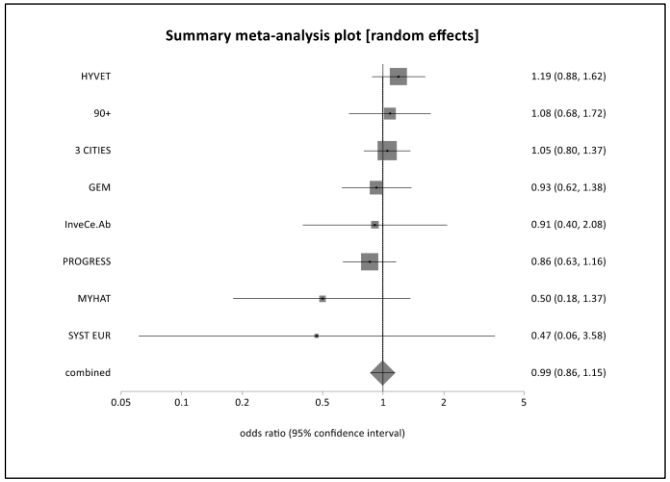


appendix-figure 2. Forest plots showing the odds ratios for risk of developing dementia by exposure to each antihypertensive class compared to no treatment in those with ≥1 year follow-up in those aged >65*.

CCB



ACE-I



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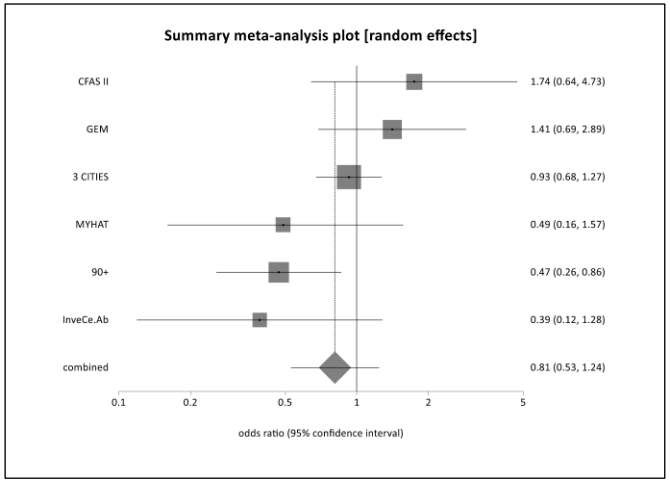

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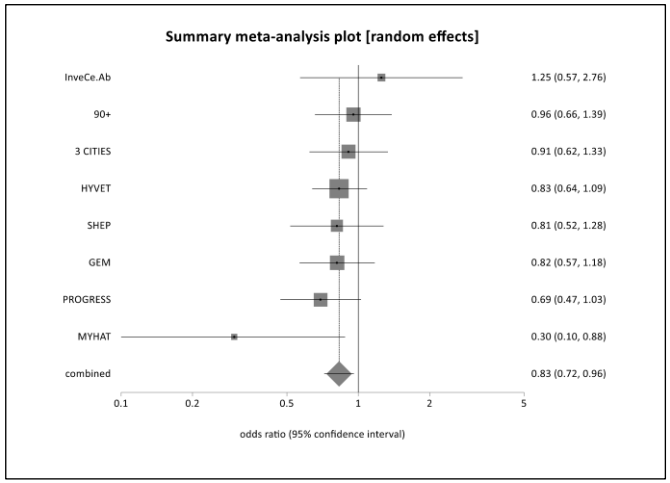

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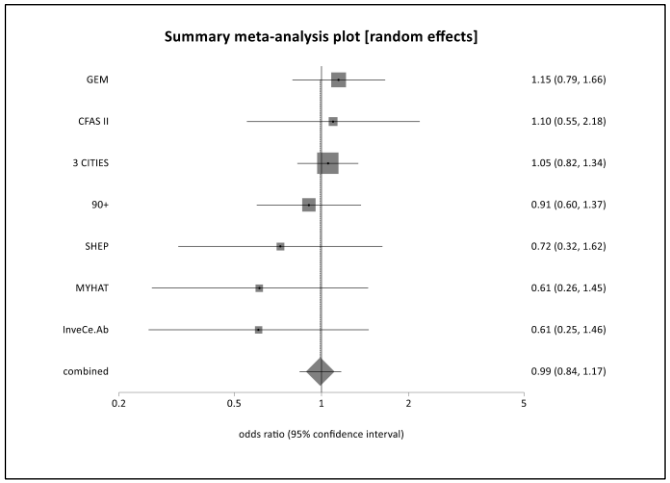
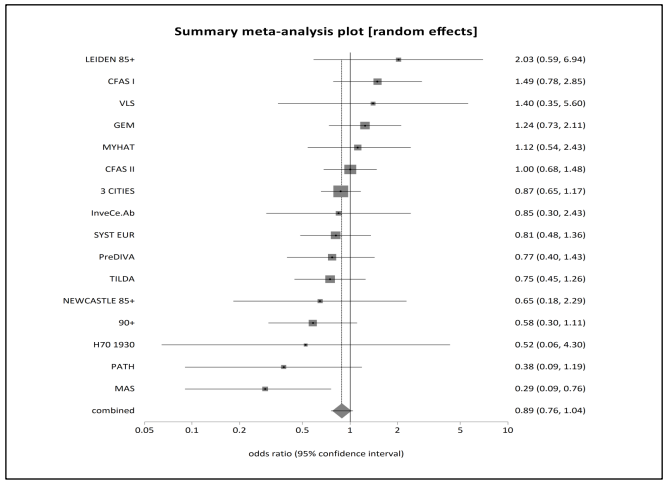


*Adjusted for sex, age, baseline systolic blood pressure and education.

Calcium Channel Blocker CCB, Angiotensin Converting Enzyme Inhibitor ACE-I,
Angiotensin Receptor Blocker ARB, Beta Blocker BB

appendix-figure 3. Forest plots showing the odds ratios for risk of developing cognitive decline by exposure to each antihypertensive class compared to no treatment in those with ≥1 year follow-up in those aged >65*†.

CCB



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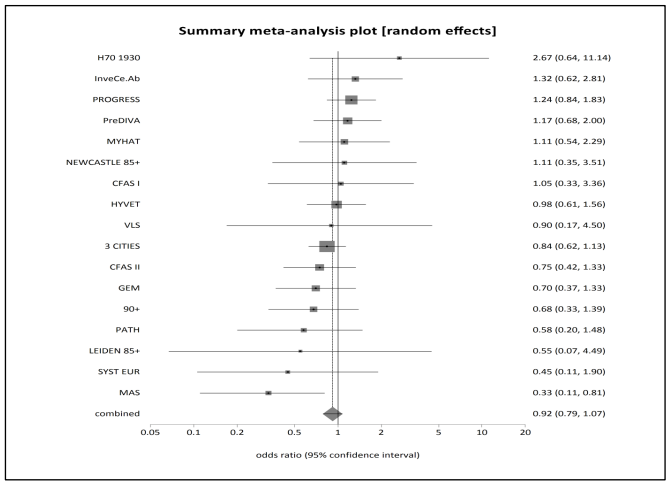
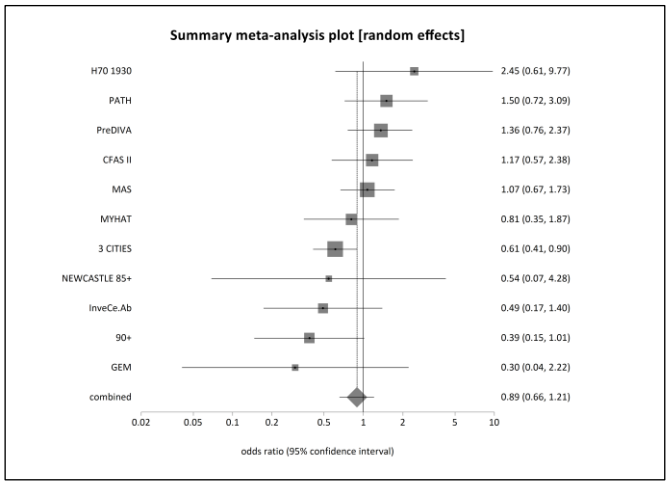


ARB



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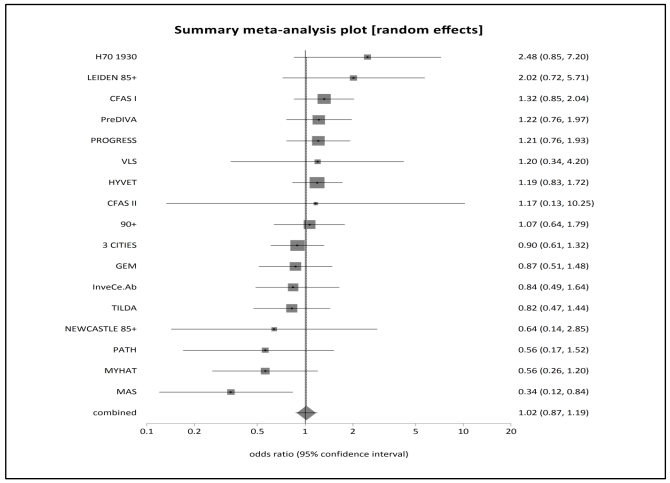
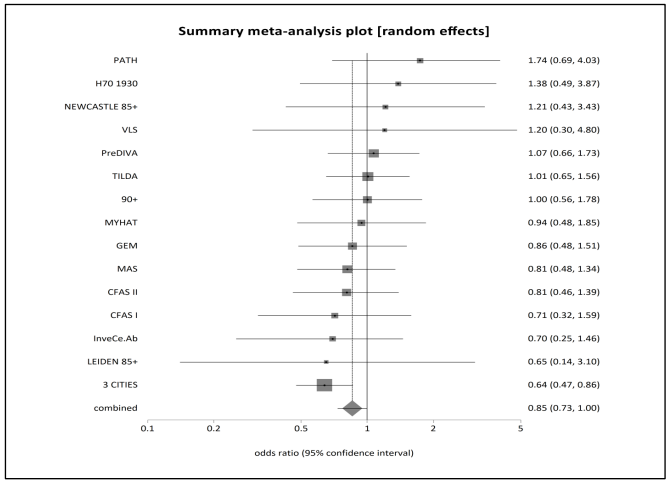


BB



†Cognitive decline classified using the reliable change index and a deterioration in the cognitive screening test, the Mini Mental State Exam (MMSE).* Adjusted for sex, age, baseline systolic blood pressure and education.

Calcium Channel Blocker CCB, Angiotensin Converting Enzyme Inhibitor ACE-I, Angiotensin Receptor Blocker ARB, Beta Blocker BB

appendix-table 1. Characteristics of analytical data sets containing participants with follow-up ≥1 year and where data were available on antihypertensive drug class,age,education,sex and baseline systolic blood pressure or presence of high blood pressure*.

Study name	Study design	Study recruitment methods and primary inclusion criteria	Total number of participants in the analytical sample	Percentage female % (n)	Mean age at baseline /years (standard deviation (SD))	Baseline systolic blood pressure (SBP) mmHg Mean (SD) / Baseline Diastolic Blood Pressure (DBP) mmHg Mean (SD) (table sorted from low to high SBP)	Mean follow-up for study sample /years (SD)	Primary decade(s) of recruitment
The Victoria Longitudinal Study (VLS)	Population cohort	Three sequential cohorts of community-dwelling adults initially aged 55-85. Visits every 4 years. Volunteers recruited via community notices and advertisements. Exclusionary criteria included dementia diagnosis,serious vascular disease,psychiatric disorder.	318	61.6% (196)	74.0 (5.6)	128 (15)/ 74 (9)	4.4 (0.5)	1980,1990,2000
The Monongahela Valley Independent Elders Survey (MY-HAT)	Population cohort	Community dwelling adults aged 65 and over. Visits every year. Recruitment via voter registration lists supplemented by volunteers from the same communities.	1187	63.7% (756)	77.4 (7.0)	133 (15)/ 74 (9)	5.0 (2.5)	2000
The Irish Longitudinal Study on Ageing (TILDA)	Population cohort	Adults aged 50 and over. Visits every 2 years. Representative stratified,clustered random sample of community-dwelling adults living in Ireland.	5095	55.8 % (2844)	61.6 (8.7)	134 (20)/82 (11)	4.4 (0.6)	2010
The Personality and Total Health study (PATH)	Population cohort	Adults age 60-64 years. Visits every 4 years. Random sample from the electoral roll.	1202	48.1% (578)	62.5 (1.5)	137 (18)/80 (10)	11.53 (1.95)	2000
The Invecchiamento Cerebrale in Abbiategrasso study (InveCe.Ab)	Population cohort	Adults aged 70-75. Visits every 2 years. Recruitment from all Abbiategrasso residents born between 1935 and 1939	1042	53.3% (555)	72.1 (1.3)	141 (17)/79 (8)	4.4 (0.6)	2010
Canadian Study of Health and Ageing (CSHA)	Population cohort	Adults age 65 and over. Visits every 5 years. Representative samples drawn from the community and institutions with equal sized samples from 5 different regions of Canada.	861	61.3% (528)	80.3 (7.4)	142 (24)/76 (13)	4.8 (0.4)	1990

Australian Longitudinal Study of Aging (ALSA)	Population cohort	Adults aged >70 years. Visits 1-3 year intervals. Sample recruited via the electoral roll.	2087	49% (1031)	78.2 (6.7)	144 (22)/77 (11)	6.5 (0.5)	1990
Sydney Memory and Ageing Study (MAS)	Population cohort	Adults aged 70-90 years. Visits every 2 years with telephone assessments in between. Sample recruited via the electoral role.	852	53.4% (455)	78.8 (4.8)	145 (20)/82 (10)	5.0 (1.5)	2000
The 3 Cities study	Population cohort	Adults aged ≥65 years and noninstitutionalised. Visits at 2 and 4 years. Sample recruited via electoral role.	6279	61.2% (3845)	73.7 (5.4)	145 (21)/82 (11)	5.3 (2.5)	2000
The Oulu 35 cohort ageing study	Population cohort	Adults aged 55. All those living in the Oulu area were invited. Visits after ~6 and 10 years.	384	60.2% (231)	63.1 (0.3)	151 (20)/87 (9)	9.2 (0.3)	1980
The Gothenburg H70 Birth Cohort Studies 1930 cohort	Population cohort	Adults aged 70 and above. Intermittent visits for up to 30 years. Sampled from the population register based on birth dates.	697	58.4 % (407)	75.6 (0.4)	151 (21)/81 (10)	6.4 (1.2)	2000
The Newcastle 85+ study	Population cohort	Adults aged 85 and who are registered with a Newcastle or North Tyneside general practice. Recruitment via general practices in Newcastle and North Tyneside Primary Care Trusts. Visits at 18 months,3 and 5 years.	400	62.8% (251)	86 (0.4)	152 (23)/75.3 (11.4)	4.5 (0.9)	2000
The Leiden 85+ study	Population cohort	Adults aged 85,recruitment was via birth cohorts living in the city of Leiden. No exclusion criteria were used. Visits every 12 months.	582	66.7% (388)	85 (0)	156 (19)/78 (10)	1 year and 5 years	2000
Cognitive Function and Ageing Study I (CFAS I)	Population cohort	Adults ≥65. Visits for subgroups at years 1,2,6,8,and for the whole sample at 10 years. Recruited via general practice records from a population catchment area around five centres.	6645	57.6% (3828)	74.6 (6.1)	Presence of hypertension	5.1 (3.9)	1980
Cognitive Function and Ageing Study II (CFAS II)	Population cohort	Adults aged 65-84. Visits at baseline and 2 years. Recruited via general practice records from a population catchment area around five centres.	4520	53.5% (2419)	74.7 (6.6)	Presence of hypertension	2.2 (0.4)	2000
The Singapore Longitudinal Aging Study (SLAS)	Selected cohort	Community dwelling Chinese adults aged 55 and over. Visits every 3 years. Door to door census.	1281	66% (845)	65.5 (7.1)	133 (16)/82 (9)	3.3 (0.5)	2000
The Kuopio Ischaemic Heart Disease risk factor study (KIHD)	Selected cohort	Adult men aged 42-60 and able to attend clinic for study visits. Visits every 4 years. Participants in the current study consisted of a representative sample of men living in the city of Kuopio and its surrounding rural communities in eastern Finland	2568	0%	57.0 (5.15)	134 (17)/89 (11)	22.8 (6.9)	1980

The 90+ study	Selected cohort	Adults aged 90 or over. Visits every 6 months. Participants were originally members of the Leisure World Cohort Study,an epidemiological health study established in the early 1980s of a California retirement community.	556	68.9% (383)	93.0 (2.6)	140 (20)/72 (11)	3.1 (2.3)	2010
The Maastricht Ageing Study (MAAS)	Selected cohort	Adults aged 24-81 (those aged >50 were selected for these analyses). Visits every 6 years. Recruitment was via a network of family practices.	926	48.8% (452)	64.9 (8.7)	142 (20)/77 (12)	10.7 (2.8)	1990
The Gothenburg H70 Birth Cohort Studies Prospective studies of women (PPSW) 1922 cohort	Selected cohort	Adults aged 70 and above. Intermittent visits for up to 30 years. Sampled from the population register based on birth dates.	275	100% (275)	70.6 (0.2)	158 (23)/83 (11)	15.6 (5.1)	1990
The Einstein Aging study (EAS)	Selected cohort	Adults aged over 70. Visits every 12 months. Potential participants were identified from Health Care Finance Administration population lists of Medicare-eligible adults or voter registration lists for Bronx County.	1311	61.8% (810)	78.5 (5.4)	Presence of hypertension	4.6 (3.4)	1990
Prevention of Dementia by Intensive Vascular Care (PreDIVA)	Selected cohort from non AHM trial data. (Cluster-randomized controlled trial with intensive vascular care versus standard care)	Community-dwelling older adults aged 70-78 years with no disorder likely to hinder successful follow-up. Visits every 2 years. Recruited from primary care.	2161	53.7% (1161)	74.2 (2.5)	153 (20) / 81 (11)	6.6 (1.2)	2010
The Ginkgo Evaluation and Memory trial (GEM)	Selected cohort from non AHM trial data. (Randomised placebo controlled trial of Ginkgo Biloba supple-mentation)	Adults aged 75 and older. Minimum clinical requirements to enter the trial,eg not taking oral anticoagulants,no diagnosis of stage III-IV heart failure. Visits every 6 months. Recruited via targeted mailing lists.	2113	53.2% (1125)	78.5 (3.2)	132.8 (17.7)/ 69.1 (9.6)	5.7 (1.5)	2000
The Perindopril Protection against Recurrent Stroke Study (PROGRESS)	Trial (Placebo controlled clinical trial (active treatment an ACE-I ± thiazide-like diuretic inhibitor))	Adults with a history of stroke or transient ischaemic attack within the previous 5 years,no indication for treatment with an ACE inhibitor and no definite contraindication for treatment with an ACE inhibitor. Visits every 6 months. Recruited from primary and secondary care clinics.	5436	30% (1631)	63.6 (9.5)	147 (19)	4.0 (0.6)	2000

The Systolic Hypertension in the Elderly Project (SHEP)	Trial (Placebo controlled trial (active treatment diuretic ± a beta blocker))	Adults aged 60 years and above with Systolic BP between 160 and 219 mmHg and diastolic BP less than 90 mmHg. Recruitment primarily via mass mailing and community screening techniques. Visits every 4 to 12 weeks.	3889	57.4% (2232)	73.9 (5.8)	171 (10)/76 (10)	4.1 (0.9)	1990
The Systolic Hypertension in Europe Trial (SYST-EUR)	Trial (Placebo controlled clinical trial (active treatment a calcium channel blocker ± an ACE inhibitor ± a diuretic))	Adults aged >60 with systolic blood pressure was 160-219 mmHg with a diastolic blood pressure lower than 95 mmHg. Recruited from primary and secondary care clinics. Visits every 3 months.	2166	65.6% (1422)	69.7 (6.3)	173 (10)/86 (6)	3.2 (1.6)	1990
The Hypertension in the Very Elderly Trial (HYVET)	Trial. (Placebo controlled clinical trial (active treatment thiazide-like diuretic ± an ACE inhibitor))	Adults aged 80 or over with sitting systolic BP 160-199 mmHg and sitting diastolic BP < 110 mmHg,no condition expected to severely limit survival,e.g. terminal illness,not resident in a nursing home and able to stand and walk. Visits every 6 months. Recruited from primary and secondary care clinics.	3021	60% (1822)	83.5 (3)	173 (9)/91 (8)	2.4 (1.4)	2000

*Table 1 is sorted by study design and baseline blood pressure.

appendix-table 2. Combined risk ratios for each antihypertensive class compared to no treatment or placebo for those aged >65 with ≥1 year follow-up

	Antihypertensive class				
	CCB	ACE-I	ARB	Diuretic	BB
Risk of developing dementia (Pooled OR 95% CI)*	0.85 (0.64:1.14)	0.99 (0.87:1.15)	0.81 (0.53:1.24)	0.83 (0.72:0.96)	0.99 (0.84:1.17)
Number of cohorts included	6	8	6	8	7
I^2 measure of heterogeneity	42.1%	0%	52%	0%	0%
Publication bias (Egger test)	P=0.0632	P=0.1263	P=0.6875	P=0.1666	P=0.0471
Risk of developing cognitive decline as measured using the Mini-Mental State Exam (MMSE) (Pooled OR 95% CI)*	0.89 (0.76:1.04)	0.92 (0.79:1.07)	0.89 (0.66:1.21)	1.02 (0.87:1.19)	0.85 (0.73:1.00)
Number of cohorts included	16	17	11	17	15
I^2 measure of heterogeneity	4.6%	0%	39.5%	11.4%	0%
Publication bias (Egger test)	P=0.5113	P=0.5202	P=0.8919	P=0.4362	P=0.0555

*Adjusted for sex,age,baseline systolic blood pressure and education.

appendix-table 3. Unadjusted pooled odds ratios calculated using the number of cases reported in the group exposed to each antihypertensive class and those exposed to no treatment or placebo for those aged >65 years.

	Risk of developing dementia (Pooled OR 95% CI)*	Risk of developing cognitive decline as measured using the Mini-Mental State Exam (MMSE) (Pooled OR 95% CI)*	Risk of developing dementia (Pooled OR 95% CI)*	Risk of developing cognitive decline as measured using the MMSE (Pooled OR 95% CI)*
	In those with ≥1 year follow-up		In those with ≥5 year follow-up	
CCB	1.01 (0.86:1.20)	0.93 (0.79:1.08)	0.93 (0.64:1.35)	0.94 (0.72:1.22)
	927 cases and 11009 without dementia	289 cases and 18,344 without cognitive decline	569 cases and 6250 without dementia	479 cases and 9704 without cognitive decline
ACE-I	1.02 (0.89:1.17)	0.94 (0.81:1.09)	1.24 (0.98:1.57)	0.96 (0.69:1.33)
	1324 and 16468	1196 and 20768	480 and 5625	381 and 6833
Diuretic	0.85 (0.74:0.98)	1.02 (0.86:1.21)	0.96 (0.66:1.39)	0.98 (0.72:1.34)
	1271 and 15237	1338 and 20307	645 and 7324	635 and 10388
BB	1.03 (0.88:1.20)	0.88 (0.77:1.00)	1.19 (0.93:1.52)	1.08 (0.80:1.44)
	974 and 12,233	1504 and 16569	621 and 6620	501 and 9470
ARB	1.08 (0.84:1.39)	0.97 (0.74:1.26)	1.01 (0.59:1.73)	1.02 (0.67:1.55)
	728 and 8535	840 and 11235	353 and 4995	254 and 4204

appendix-table 4: Pooled odds ratios for risk of developing dementia and cognitive decline comparing exposure to each antihypertensive drug class with exposure to other drug classes in those with ≥1 year follow-up and aged >65 years.

	Antihypertensive class				
	CCB	ACE-I	ARB	Diuretic	BB
Risk of developing dementia (Pooled OR 95% CI)*	0.91 (0.76:1.09)	0.88 (0.73:1.07)	0.96 (0.67:1.38)	0.77 (0.54:1.11)	1.06 (0.88:1.26)
Number of cohorts included	6	6	6	5	6
I^2 measure of heterogeneity	0%	0%	41.8%	62.6%	0%
Publication bias (Egger test)	P=0.7282	P=0.7215	P=0.594	P=0.14	P=0.3766
Risk of developing cognitive decline as measured using the Mini-Mental State Exam (MMSE) (Pooled OR 95% CI)*	1.05 (0.89:1.24)	0.96 (0.78:1.18)	0.86 (0.65:1.13)	0.98 (0.82:1.18)	0.95 (0.80:1.12)
Number of cohorts included	15	14	11	14	15
I^2 measure of heterogeneity	1.4%	14.4%	23.5%	0%	36.5%
Publication bias (Egger test)	P=0.3638	P=0.9332	P=0.3881	P=0.5171	P=0.678

*Adjusted for sex,age,baseline systolic blood pressure or presence of hypertension and education.

appendix-table 5. Unadjusted pooled odds ratios calculated using the number of cases reported in the group exposed to each antihypertensive class and those exposed to other antihypertensive treatment for those aged >65 years.

	Risk of developing dementia (Pooled OR 95% CI)*	Risk of developing cognitive decline as measured using the Mini-Mental State Exam (MMSE) (Pooled OR 95% CI)*	Risk of developing dementia (Pooled OR 95% CI)*	Risk of developing cognitive decline as measured using the MMSE (Pooled OR 95% CI)*
	In those with ≥1 year follow-up		In those with ≥5 year follow-up	
CCB	0.84 (0.66:1.07)	0.91 (0.75:1.11)	0.72 (0.46:1.13)	0.86 (0.59:1.24)
	681 cases and 7572 without dementia	810 cases and 13242 without cognitive decline	366 cases and 3654 without dementia	285 cases and 6155 without cognitive decline
ACE-I	0.85 (0.64:1.14)	0.87 (0.69:1.10)	0.97 (0.69:1.37)	1.04 (0.68:1.60)
	681 and 7572	737 and 12522	323 and 3568	263 and 5756
Diuretic	0.71 (0.35:1.44)	1.06 (0.85:1.31)	0.87 (0.46:1.65)	0.85 (0.62:1.17)
	643 and 5170	722 and 12617	235 and 3635	287 and 6114
BB	0.94 (0.76:1.19)	0.96 (0.75:1.23)	1.14 (0.84:1.56)	0.88 (0.51:1.54)
	681 and 7574	810 and 13320	328 and 3667	303 and 6059
ARB	0.69 (0.41:1.18)	0.92 (0.68:1.25)	0.72 (0.46:1.11)	0.87 (0.44:1.72)
	703 and 7549	648 and 10416	318 and 3560	132 and 2491

appendix-table 6. Pooled odds ratios for risk of cognitive decline in memory and attention tasks,(from neuropsychological tests),compared to those without AHM or placebo, for those aged >65 years.

	Attention* (≥1 year follow-up) OR 95% CI 4 cohorts	Attention (≥5 year follow-up) OR 95% CI 3 cohorts	Memory** (≥1 year follow-up) OR 95% CI 7 cohorts	Memory (≥5 year follow-up) OR 95% CI 5 cohorts
CCB	1.46 (0.78:2.76)	1.47 (0.65:3.33)	1.26 (0.81:1.84)	1.47 (0.80:2.69)
ACE-I	1.00 (0.42:2.39)	1.07 (0.34:3.37)	0.98 (0.71:1.36)	1.16 (0.77:1.75)
Diuretic	1.04 (0.61:1.78)	1.22 (0.61:2.47)	1.09 (0.73:1.64)	1.05 (0.55:1.98)
BB	0.96 (0.75:1.23)	1.20 (0.63:2.29)	1.53 (1.04:2.27)	1.17 (0.61:2.24)
ARB	0.77 (0.55:1.09)	0.91 (0.39:2.14)	1.11 (0.78:1.64)	0.78 (0.36:1.69)

*Trail Making Test B

**Varied standard recall tests

Adjusted for sex,age,baseline systolic blood pressure or presence of hypertension and education. Additional adjustment for ethnic group in the Einstein Aging Study (EAS)

appendix-table 7. Pooled odds ratios for risk of developing incident dementia or cognitive decline in those aged 65 and under compared to those without AHM or placebo.

	Risk of developing dementia (Pooled OR 95% CI)*	Risk of developing cognitive decline as measured using the Mini-Mental State Exam (MMSE) (Pooled OR 95% CI)*	Risk of developing dementia (Pooled OR 95% CI)*	Risk of developing cognitive decline as measured using the Mini-Mental State Exam (MMSE) (Pooled OR 95% CI)*
	In those with ≥1 year follow-up		In those with ≥5 year follow-up	
CCB	Insufficient data	1.51 (0.60:3.81)	Insufficient data	0.46 (0.15:1.40)
ACE-I	Insufficient data	1.14 (0.66:1.97)	Insufficient data	Insufficient data
Diuretic	0.95 (0.46:1.93)	1.06 (0.42:2.68)	Insufficient data	1.04 (0.65:1.65)
BB	Insufficient data	1.03 (0.53:2.01)	Insufficient data	1.44 (0.68:3.07)
ARB	Insufficient data	Insufficient data	Insufficient data	Insufficient data

*Adjusted for sex,age,baseline systolic blood pressure or presence of hypertension and education. Additional adjustment for ethnic group in the Einstein Aging Study (EAS

appendix-table 8:. Pooled odds ratios and associated 95% confidence intervals for AHM use compared to no treatment or to placebo, in those aged >65

		Risk of developing dementia (Pooled OR 95% CI)	Risk of developing dementia (Pooled OR 95% CI)	Risk of developing cognitive decline as measured using the Mini-Mental State Exam (MMSE) ǂ (Pooled OR 95% CI)	Risk of developing cognitive decline as measured using the Mini-Mental State Exam (MMSE) ǂ (Pooled OR 95% CI)
		For those with ≥1 year follow-up	For those with ≥5 year follow-up	For those with ≥1 year follow-up	For those with ≥5 year follow-up
RCT	Unadjusted	0.88 (0.74:1.04)	0.67 (0.52:0.85)	0.97 (0.74:1.26)	0.29 (0.10:0.79)
	Adjusted*	0.86 (0.72:1.02)	0.65 (0.51:0.82)	0.95 (0.66:1.37)	0.44 (0.15:1.25)
		4 trials	3 trials	3 trials	2 trials
Cohort studies	Unadjusted	1.116 (0.952:1.307)	1.18 (0.78:1.78)	0.98 (0.82:1.11)	1.04 (0.84:1.29)
	Adjusted**	1.12 (0.98:1.28)	1.12 (0.74:1.70)	0.87 (0.75:1.01)	1.01 (0.78:1.31)
		7 cohorts	9 cohorts	15 cohorts	14 cohorts

*Adjusted for sex,age,baseline systolic blood pressure or presence of hypertension and education. **Additional adjustment for ethnic group in the Einstein Aging Study (EAS)

ǂ MMSE decline calculated using the Reliable Change Index (RCI).

appendix-table 9. Antihypertensive use compared to no antihypertensive use, or placebo, meta-analyses by sex in those aged >65 years.

			Male	Female
In those with ≥1 year follow-up	Cognitive decline (MMSE)	Combined odds Ratio*	0.88 (0.70:1.11)	0.90 (0.73:1.10)
		Publication bias (Egger's test)	P=0.2499	P=0.4543
		Heterogeneity I2	1%	0%
		Number of cohorts	9	9
	Dementia	Combined odds Ratio*	0.82 (0.66:1.01)	0.86 (0.70:1.06)
		Publication bias (Egger's test)	P=0.6776	P=0.8929
		Heterogeneity I2	0%	0%
		Number of cohorts	7	7
In those with ≥5 year follow-up	Cognitive decline (MMSE)	Combined odds Ratio*	0.56 (0.32:1.00)	1.00 (0.65:1.53)
		Publication bias (Egger's test)	P=0.4675	P=0.1234
		Heterogeneity I2	32.4%	50.4%
		Number of cohorts	9	9
	Dementia	Combined odds Ratio*	1.26 (0.54:2.96)	0.98 (0.45:2.17)
		Publication bias (Egger's test)	P=0.507	P=0.2525
		Heterogeneity I2	68.4%	73.5%
		Number of cohorts	6	6

*Adjusted for age,education and baseline systolic blood pressure or presence of hypertension

appendix A Search Strategy

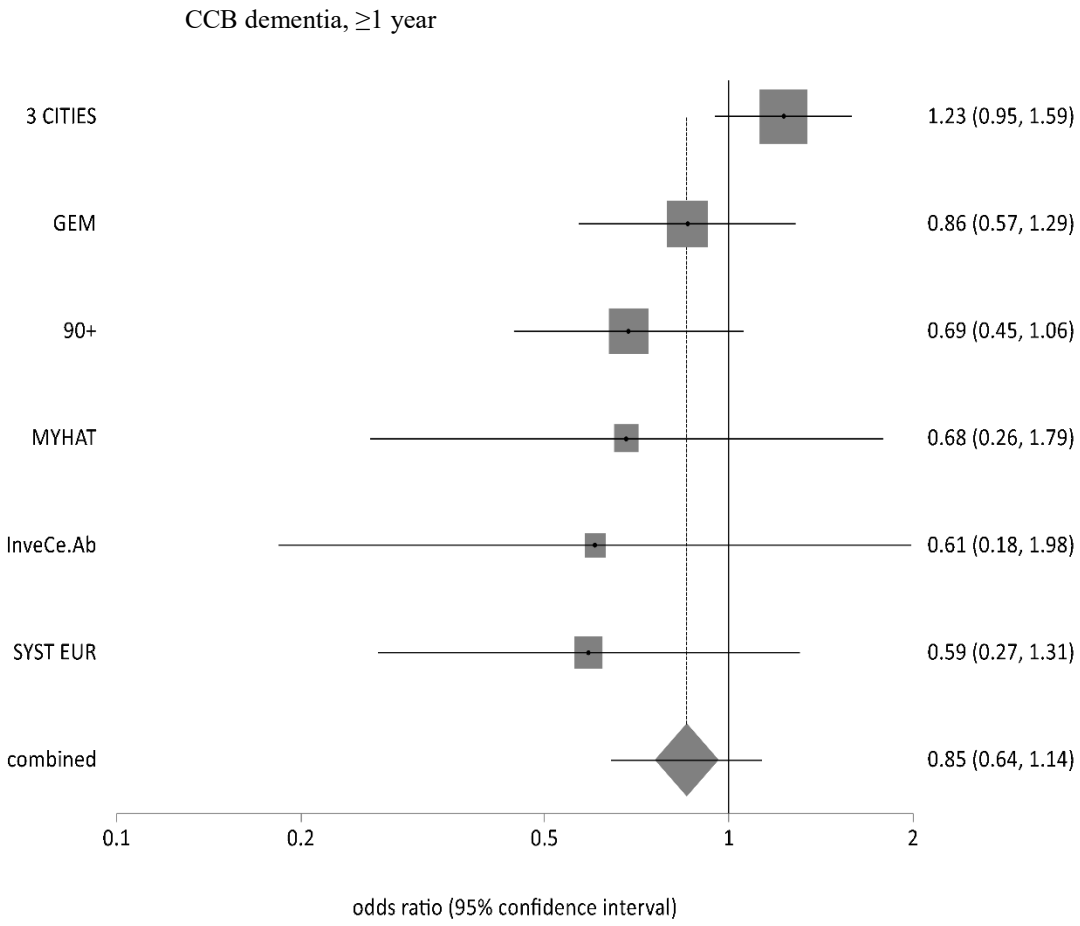
The databases Embase, PsycINFO®, Medline, Medline In-Process and other non-indexed citations and PubMed to be searched using the search terms:

(dementia OR cognit* OR mild cognitive impairment OR Alzheimer disease OR dementia vascular OR dementia multi-infarct) AND (antihypertensives OR antihypertensive agents OR diuretic OR diuretics OR thiazide OR thiazide-like OR calcium channel blocker OR calcium channel blockers OR calcium antagonist OR angiotensin converting enzyme inhibitor OR angiotensin-converting enzyme inhibitors OR ACE inhibitors OR angiotensin receptor blocker OR angiotensin receptor blockers OR ARB OR beta blocker OR adrenergic beta-antagonist

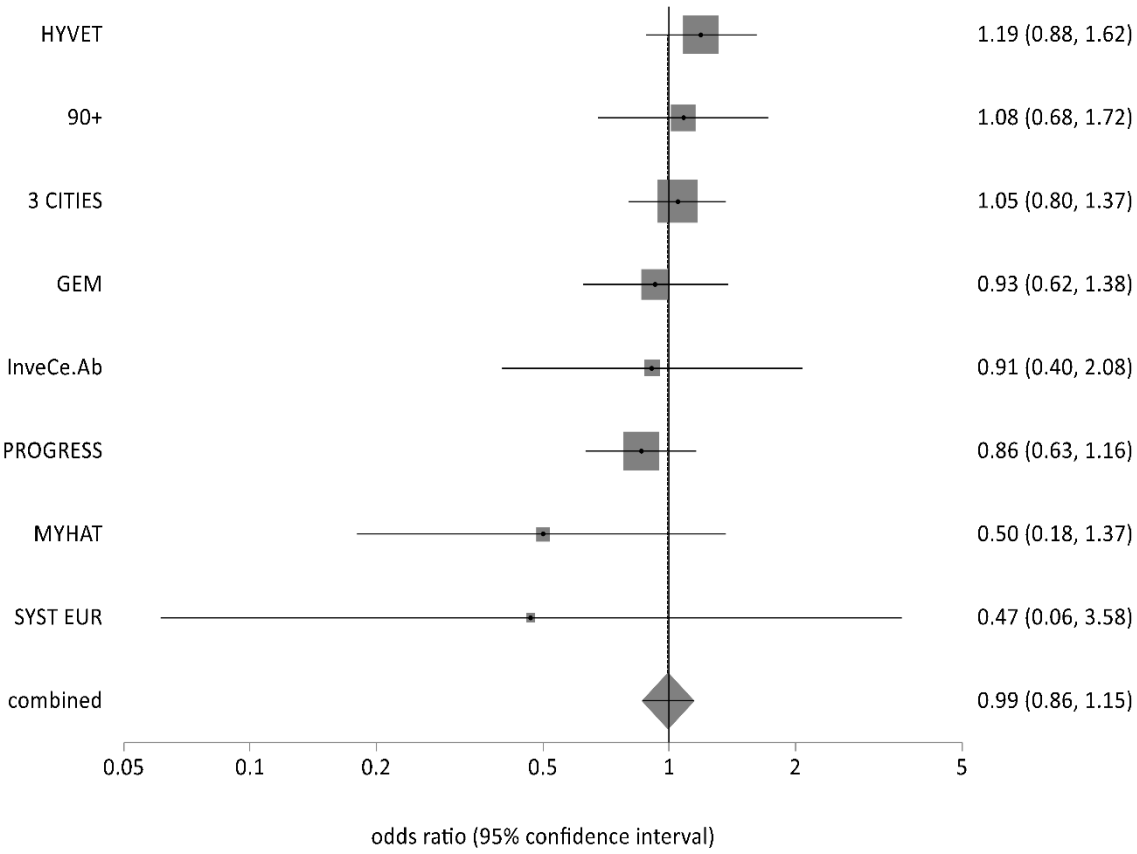
Search strategy advice from Dr Andrew Booth, Reader in evidence based information practice and director of information. School of Health and Related Research. University of Sheffield , UK. Qualifications of searchers: Dr R Peters, BSc, MSc, PhD, Dr J Peters FFPHM, BTech, MPH, PhD.

appendix B Forest plots

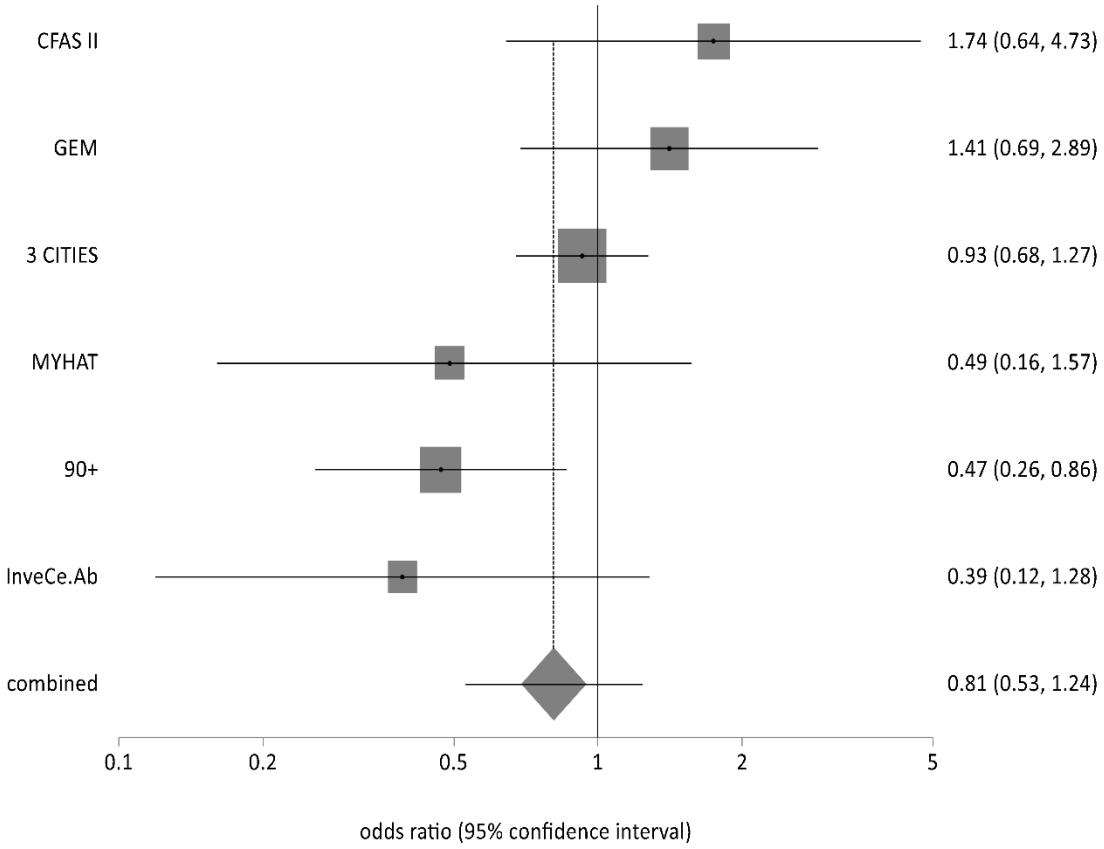
Antihypertensive class compared to no treatment or placebo in those aged >65 years.



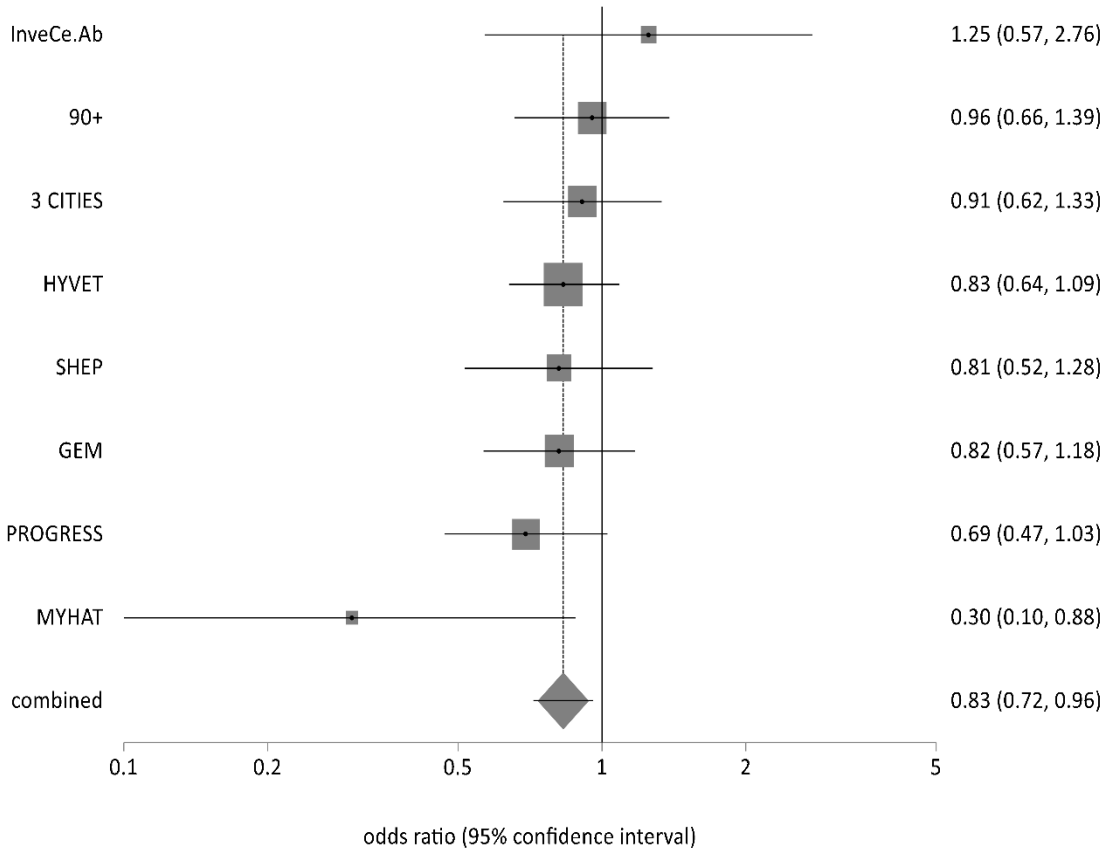
ACE-I, dementia, ≥1 year



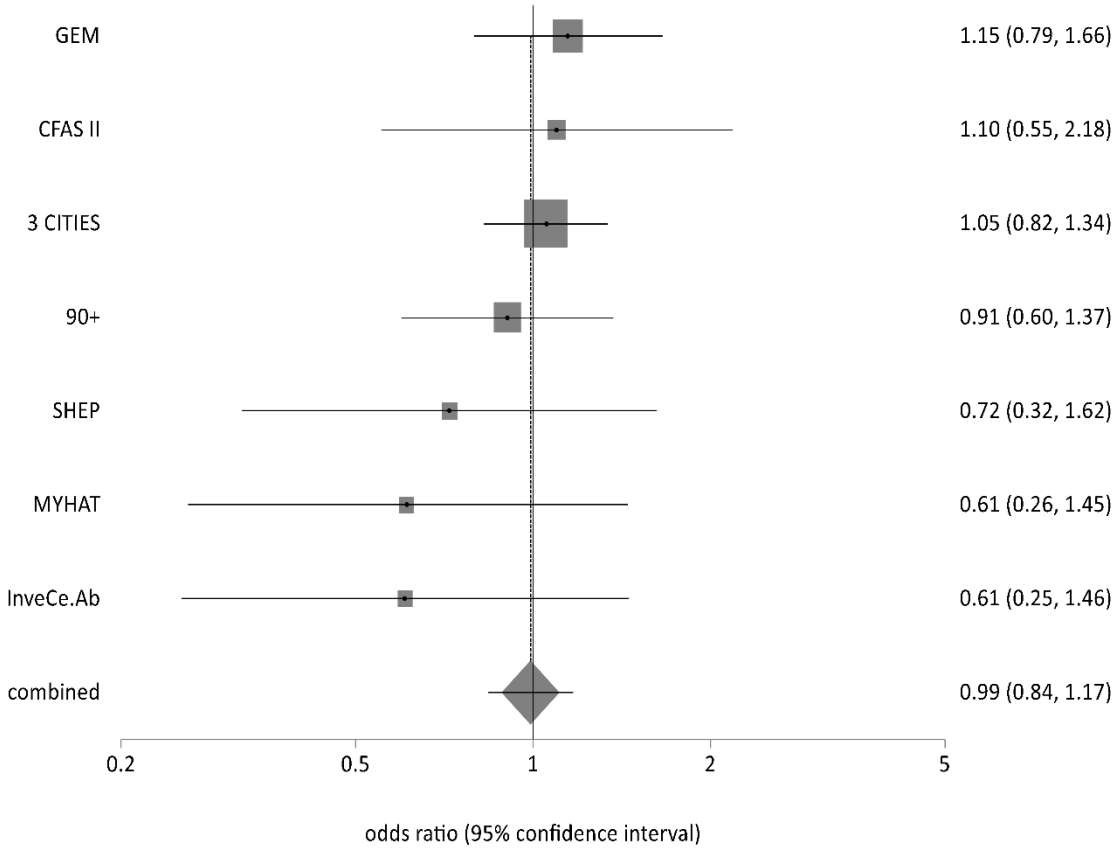
ARB, dementia, ≥1 year



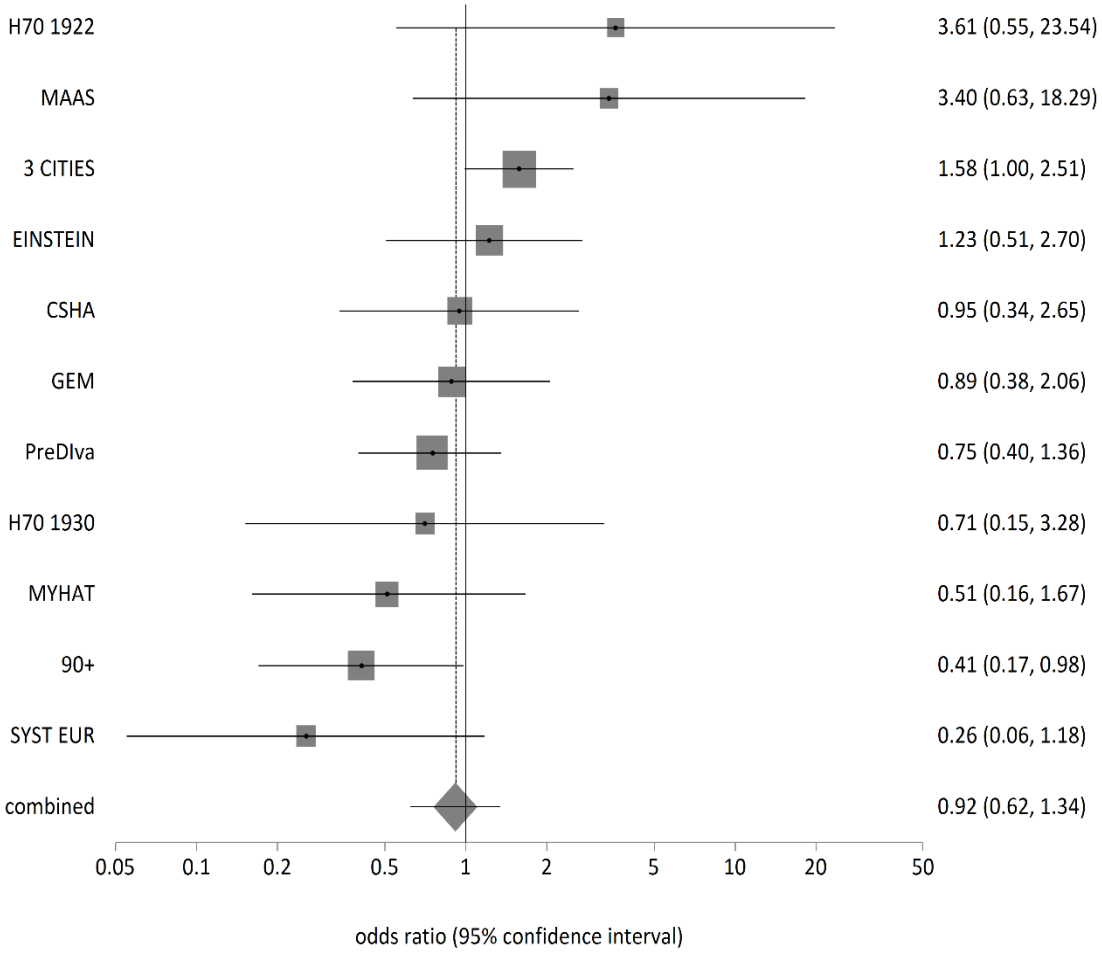
Diuretic, dementia, ≥1 year



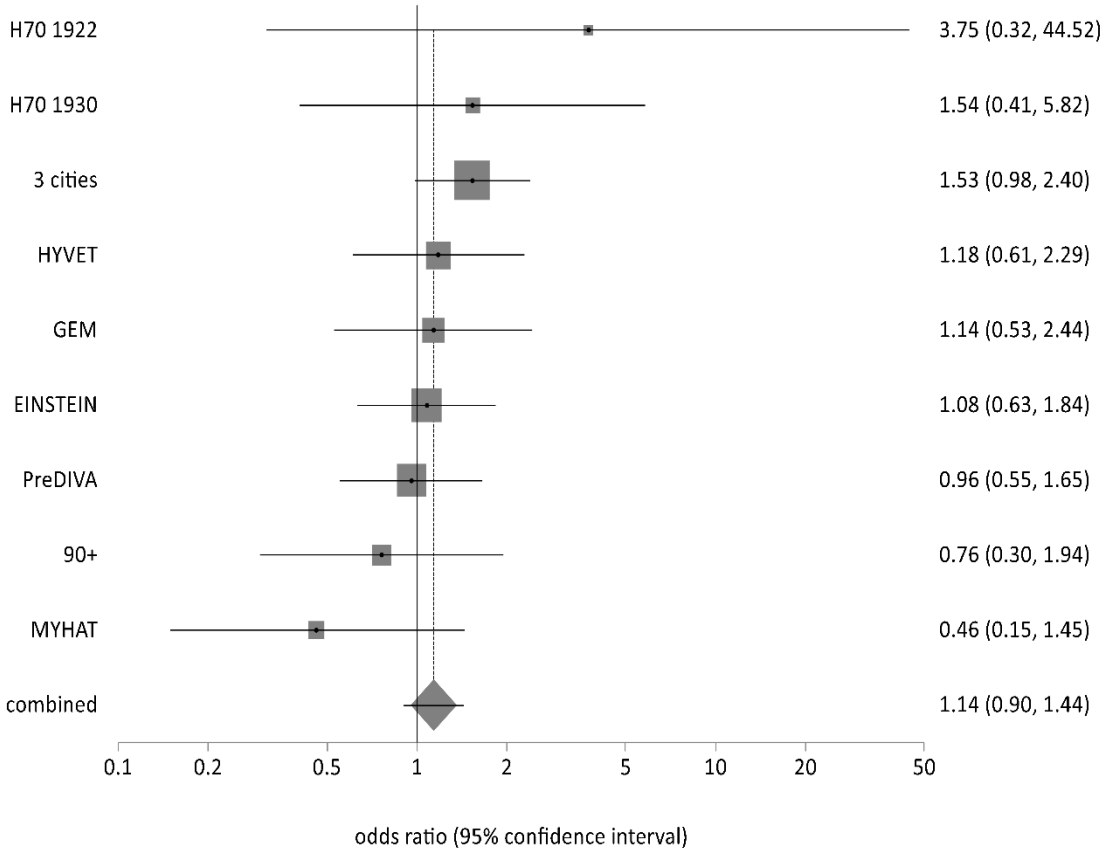
BB, dementia, ≥1 year



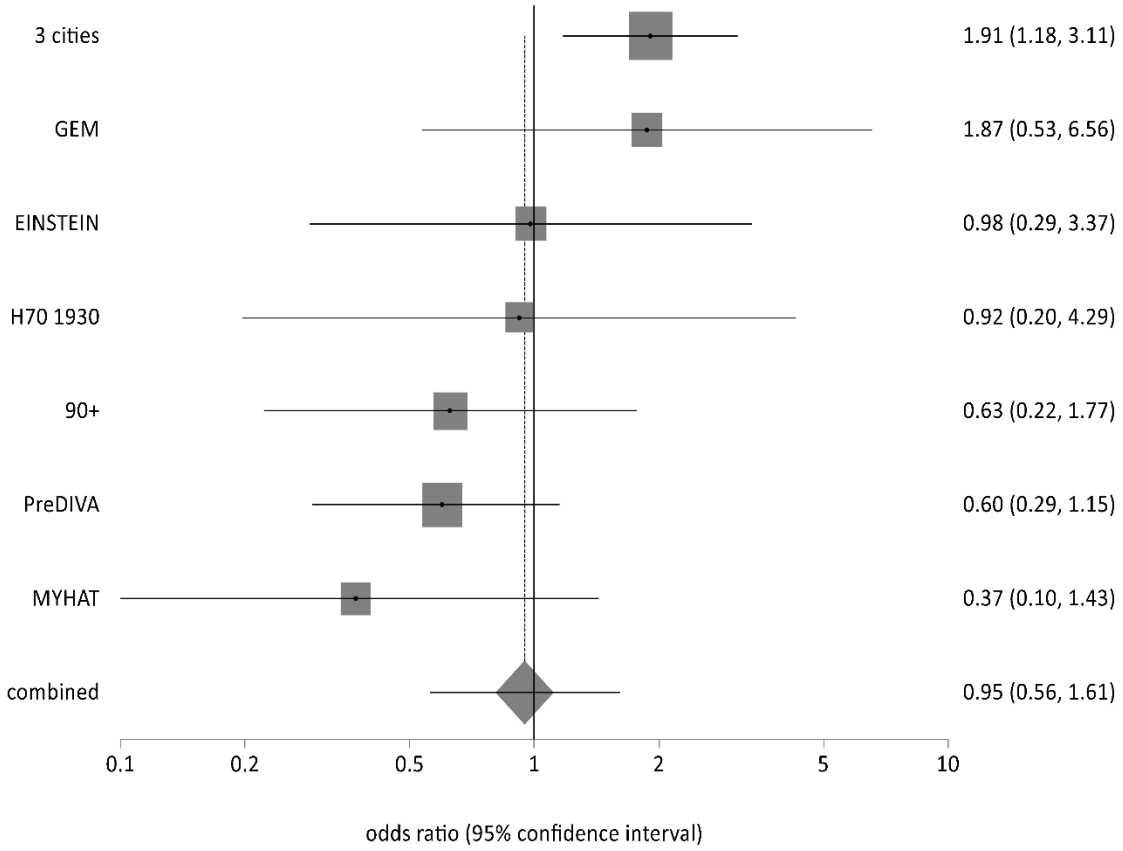
CCB, dementia, ≥5 years



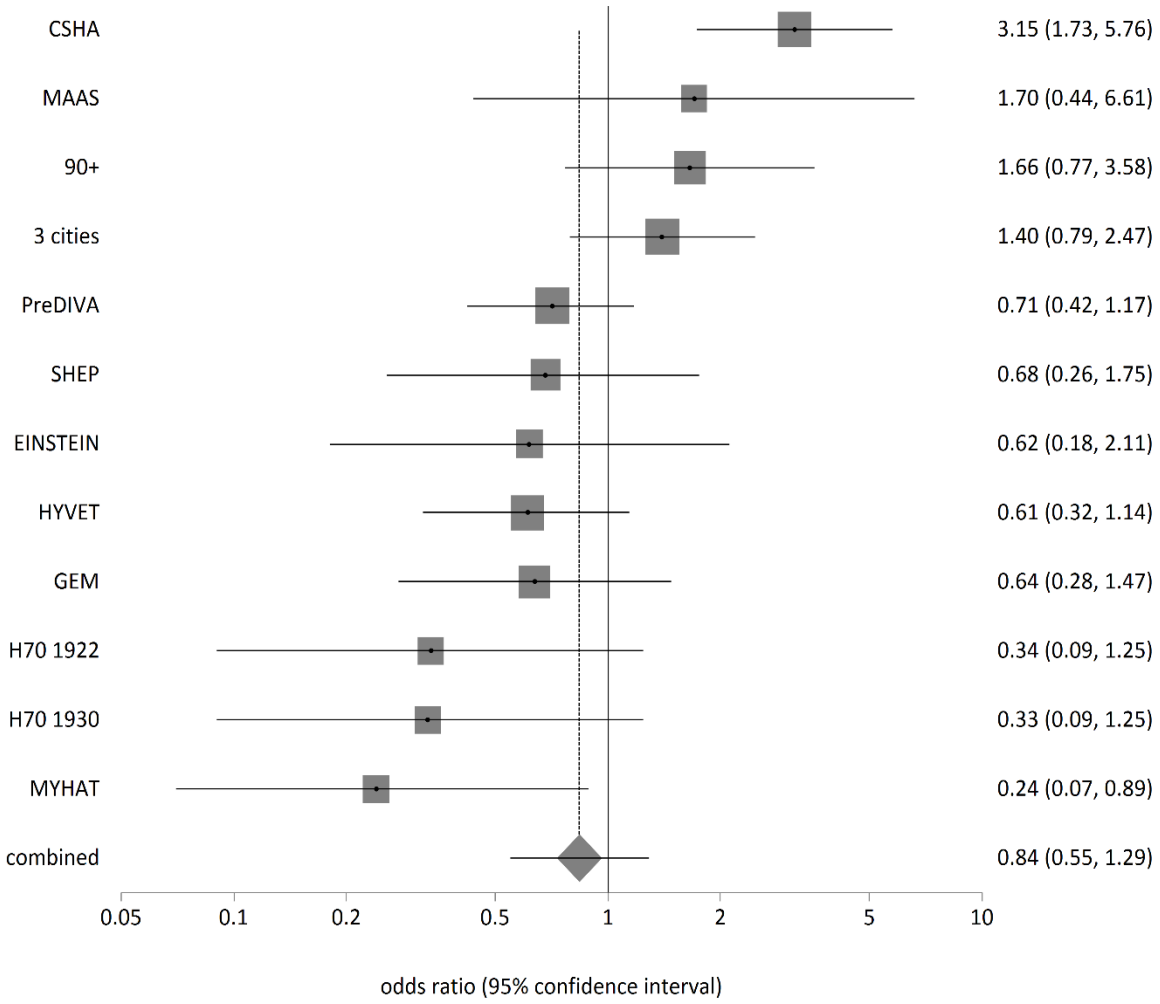
ACE-I, dementia, ≥5 year



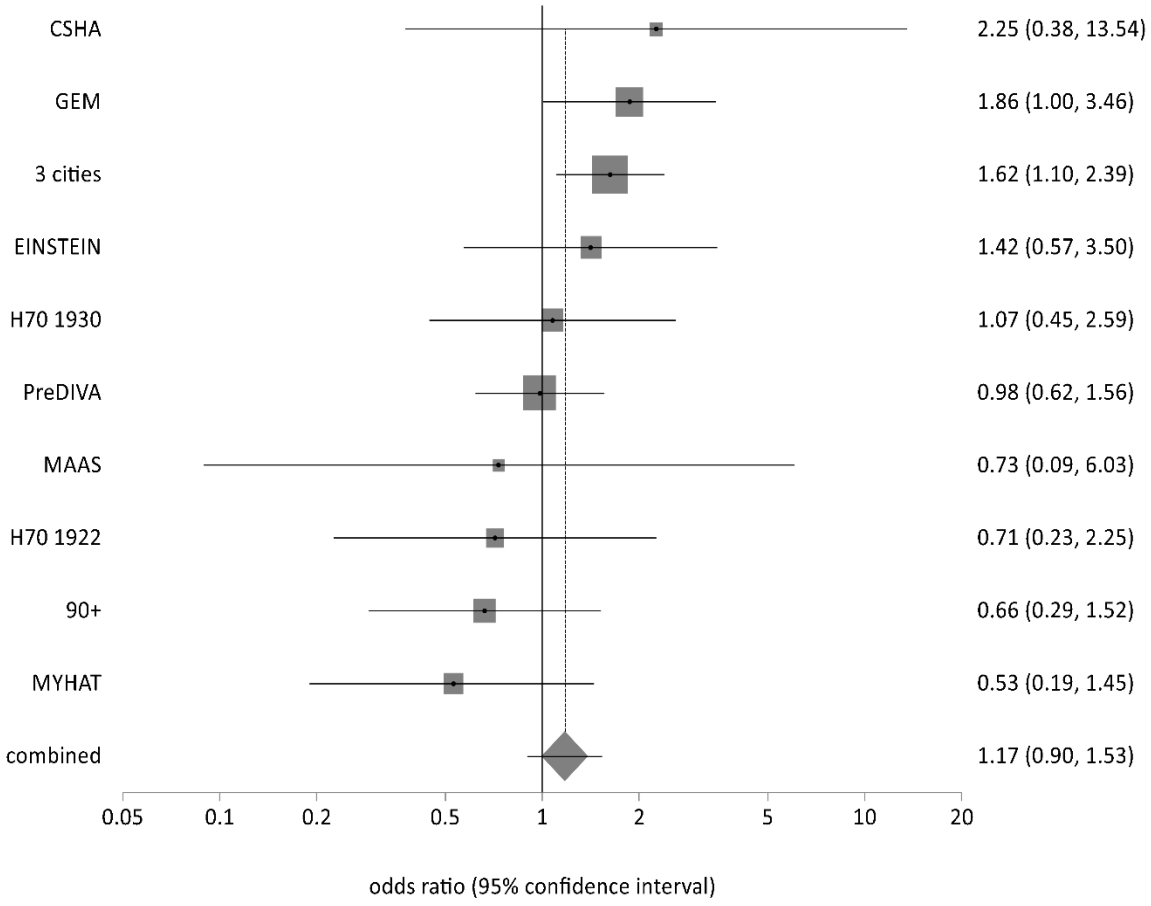
ARB, dementia, ≥5 years



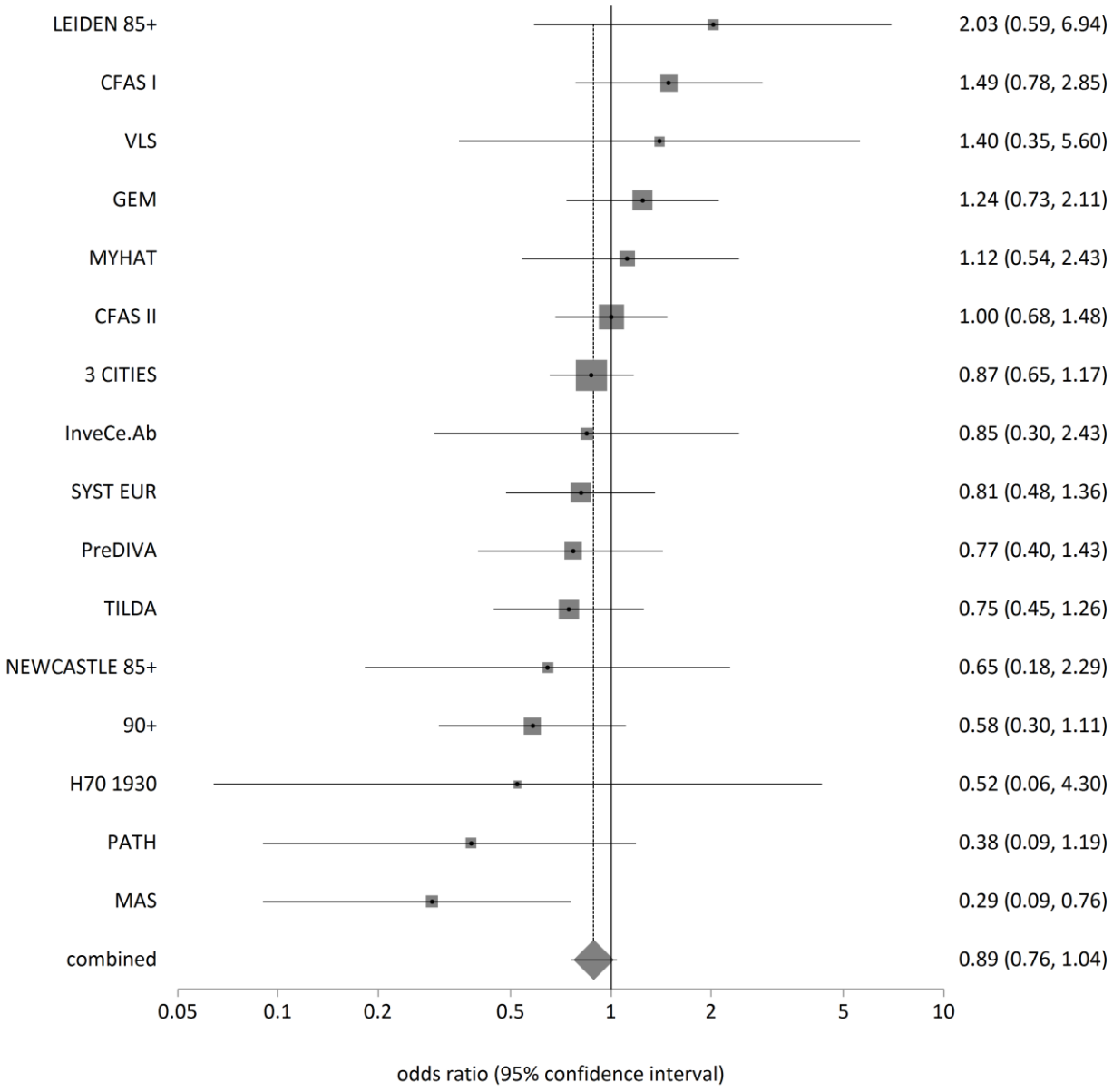
Diuretic, dementia, ≥5 years



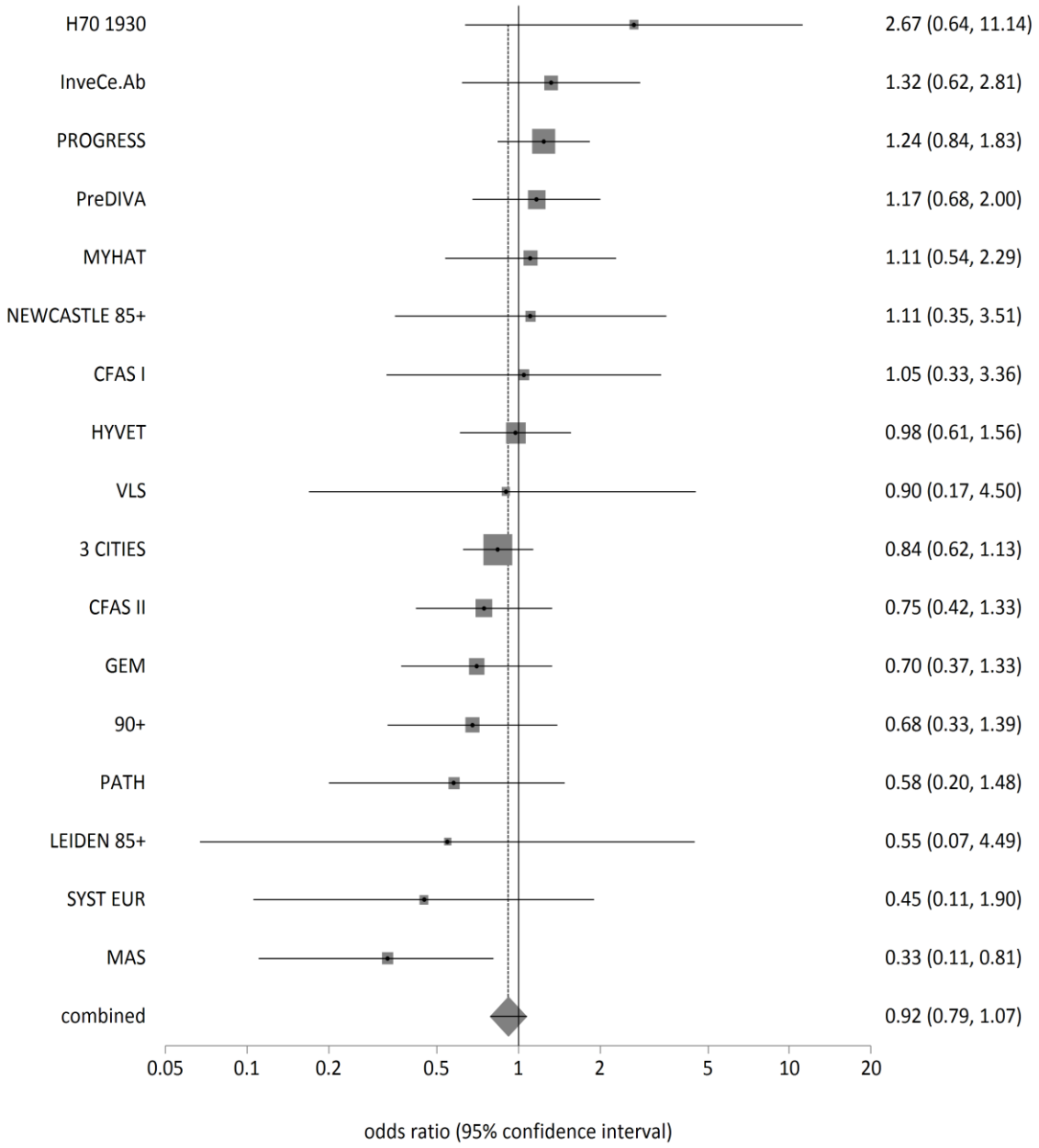
BB, dementia, ≥5 years



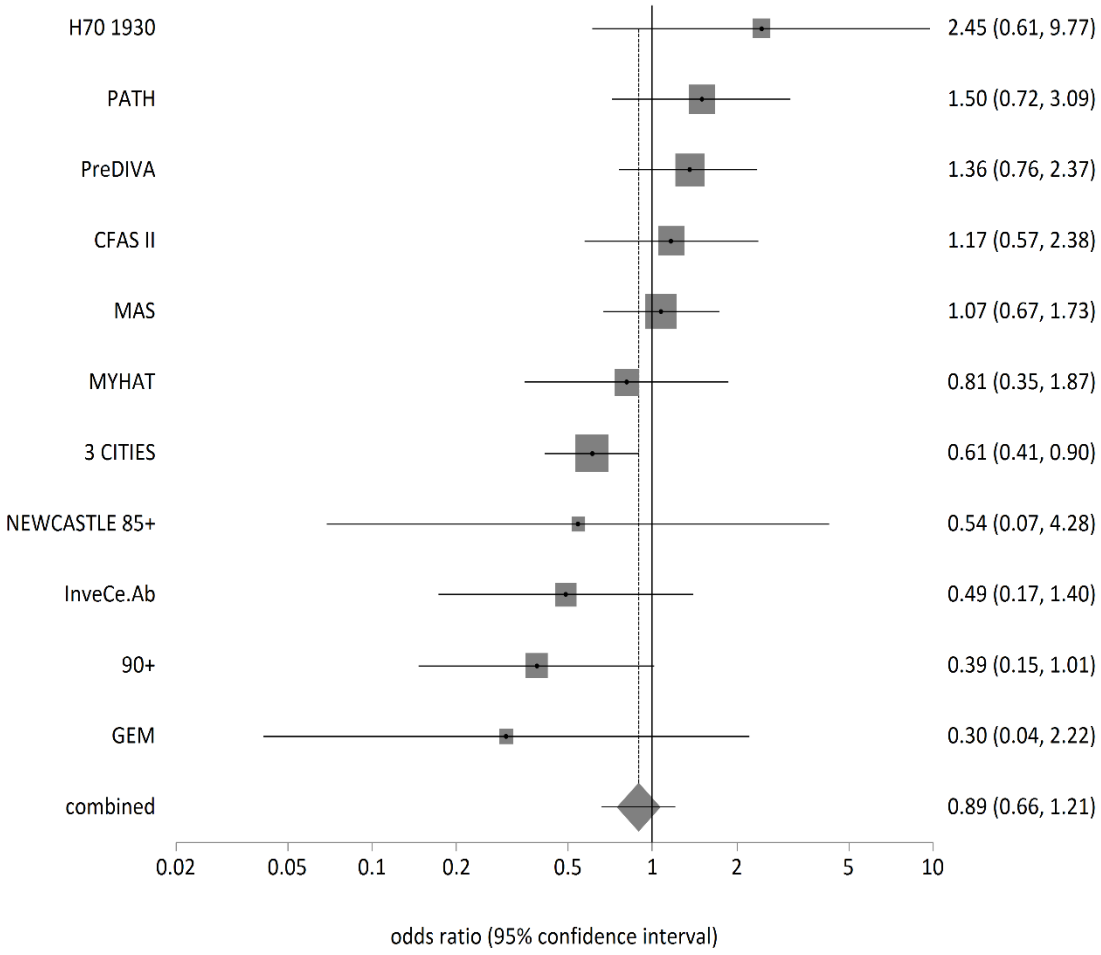
CCB, MMSE cognitive decline, ≥1 year



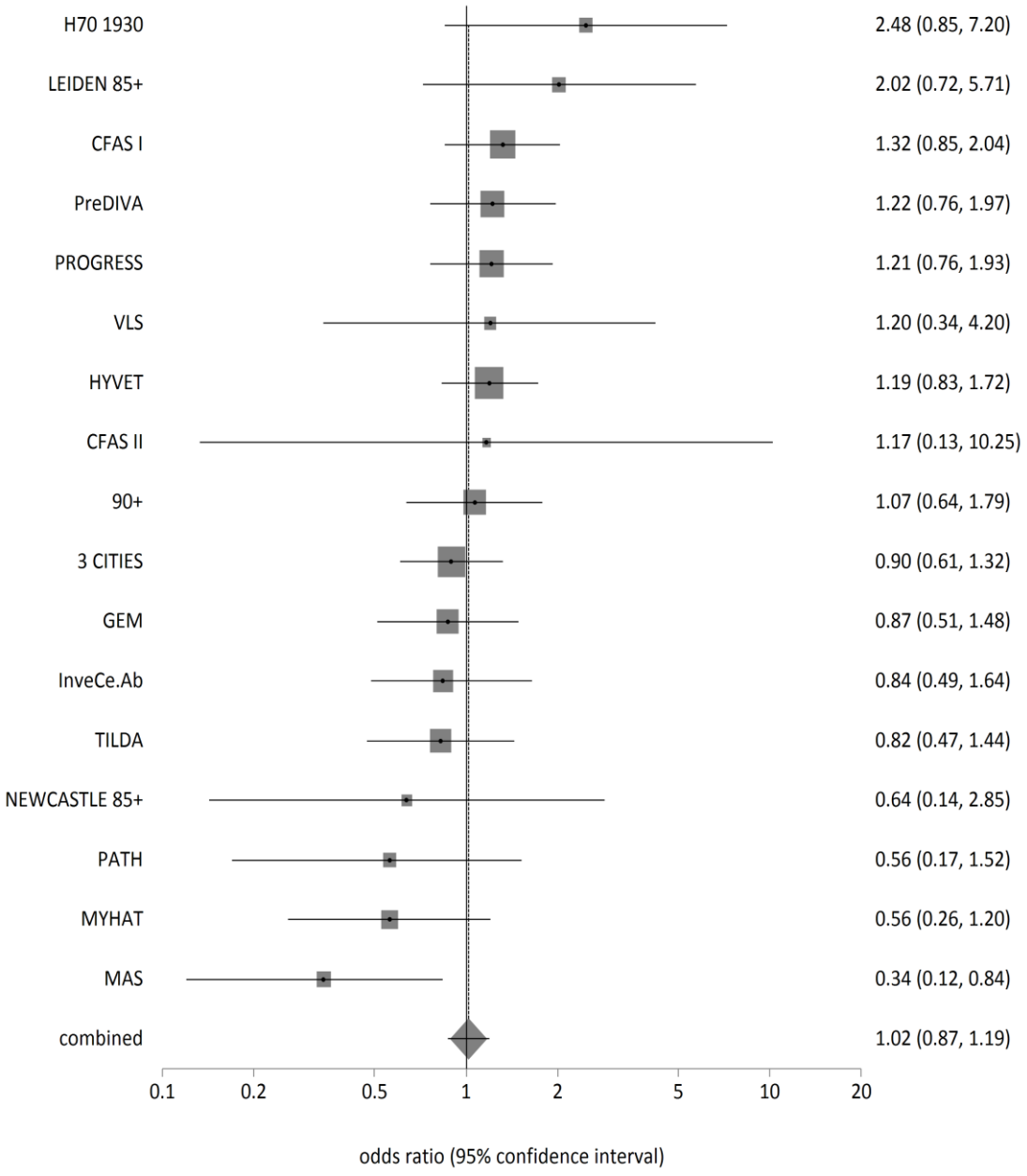
ACE-I, MMSE cognitive decline, ≥1 year



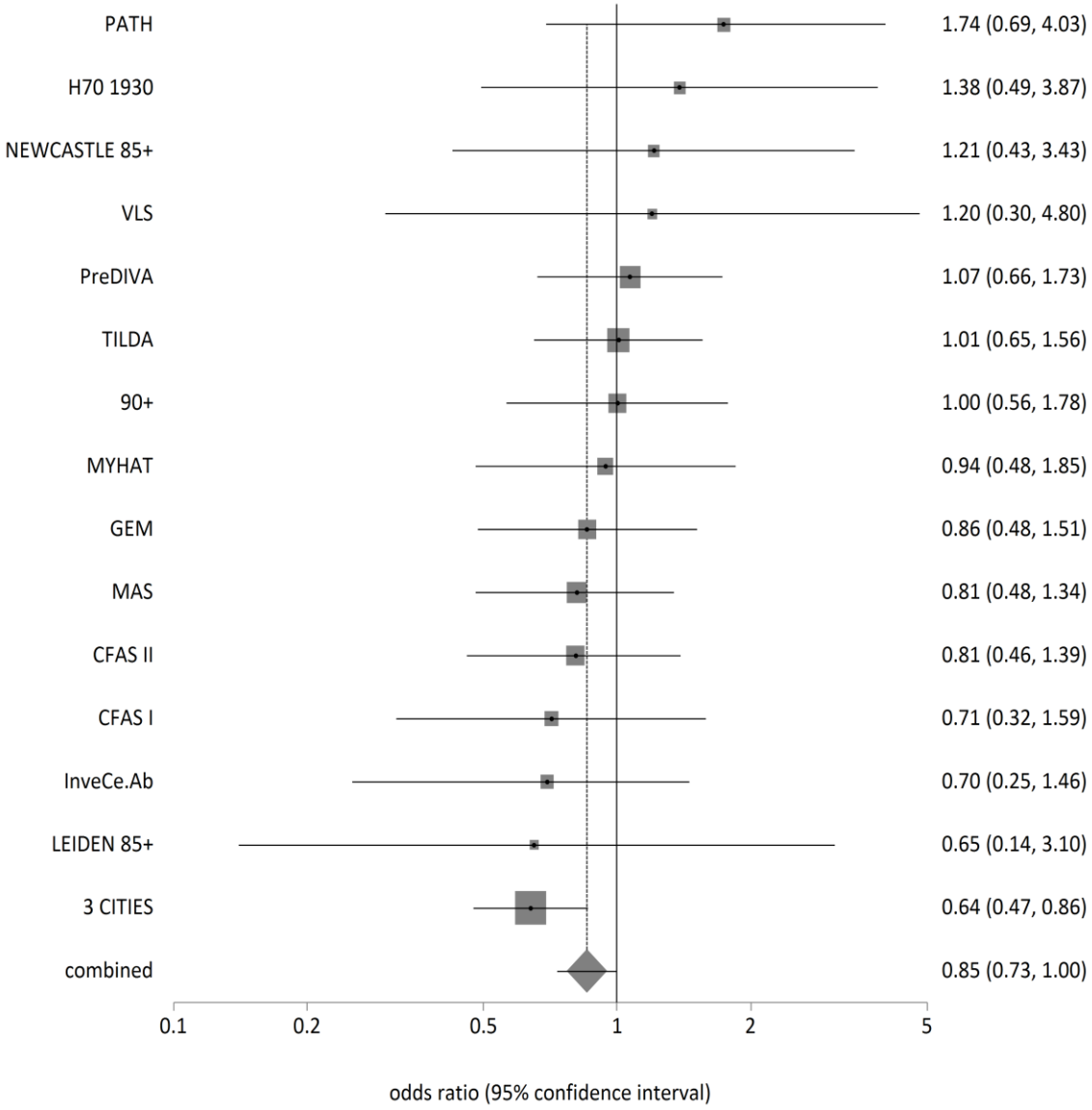
ARB, MMSE cognitive decline, ≥1 year



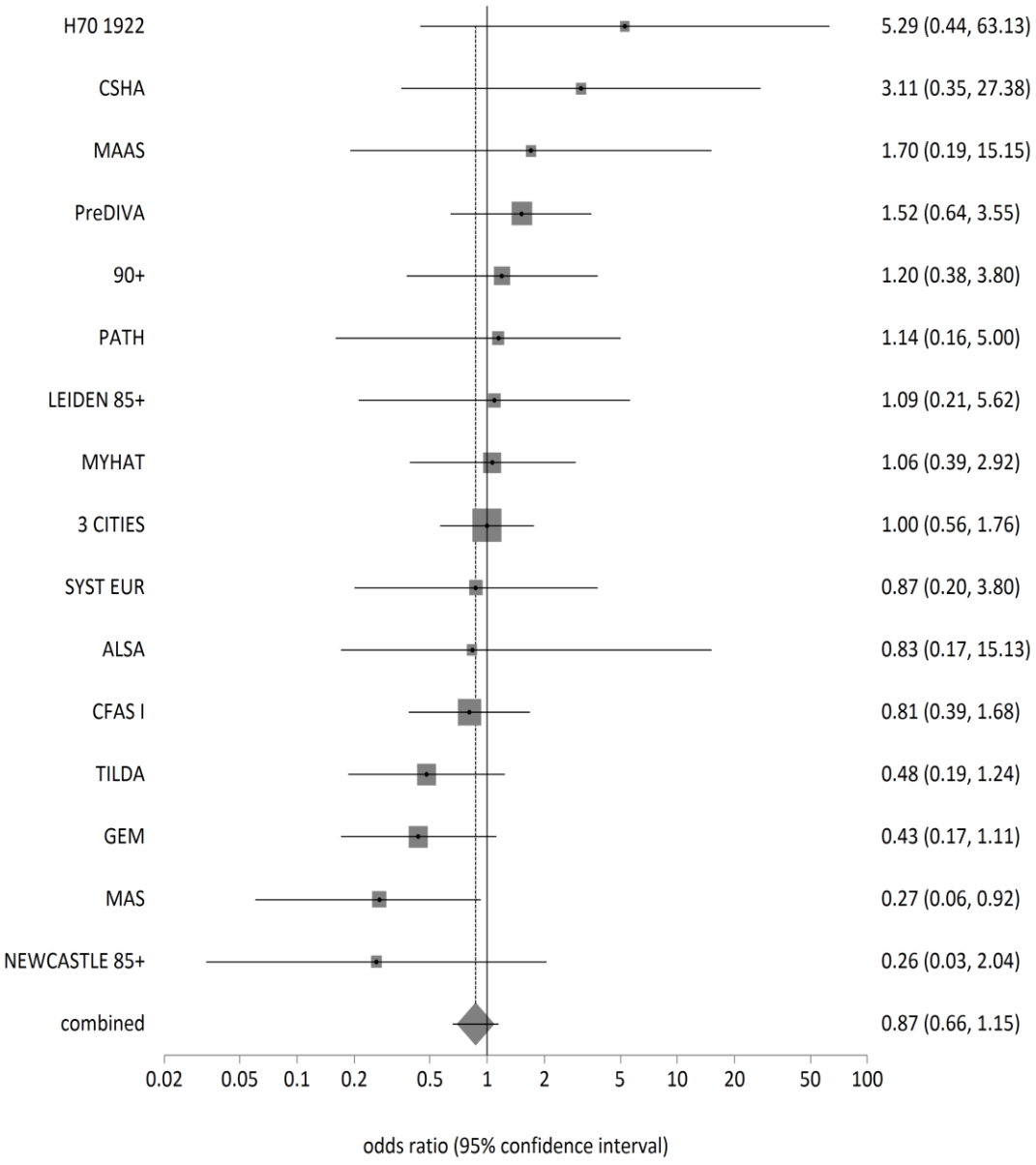
Diuretic, MMSE cognitive decline, ≥1 year



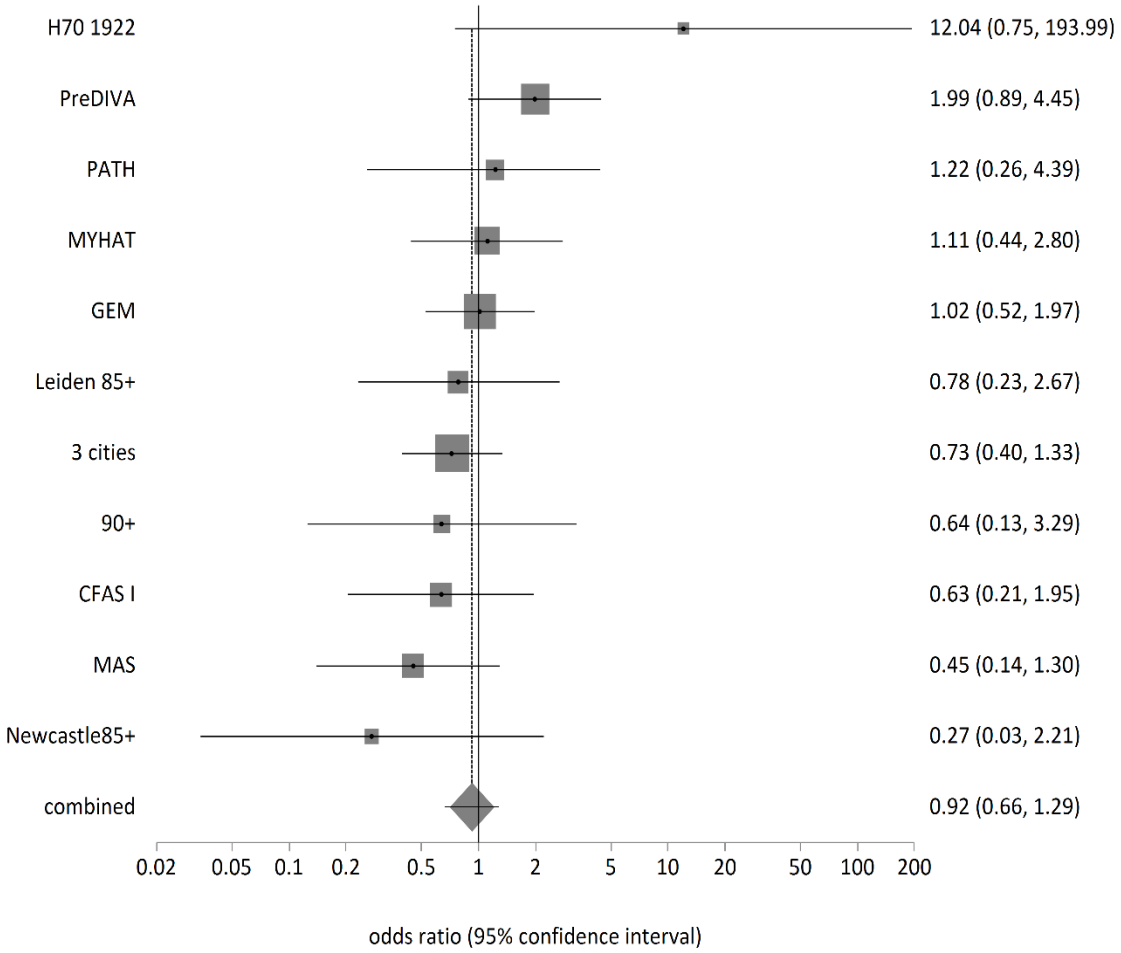
BB, MMSE cognitive decline, ≥1 year



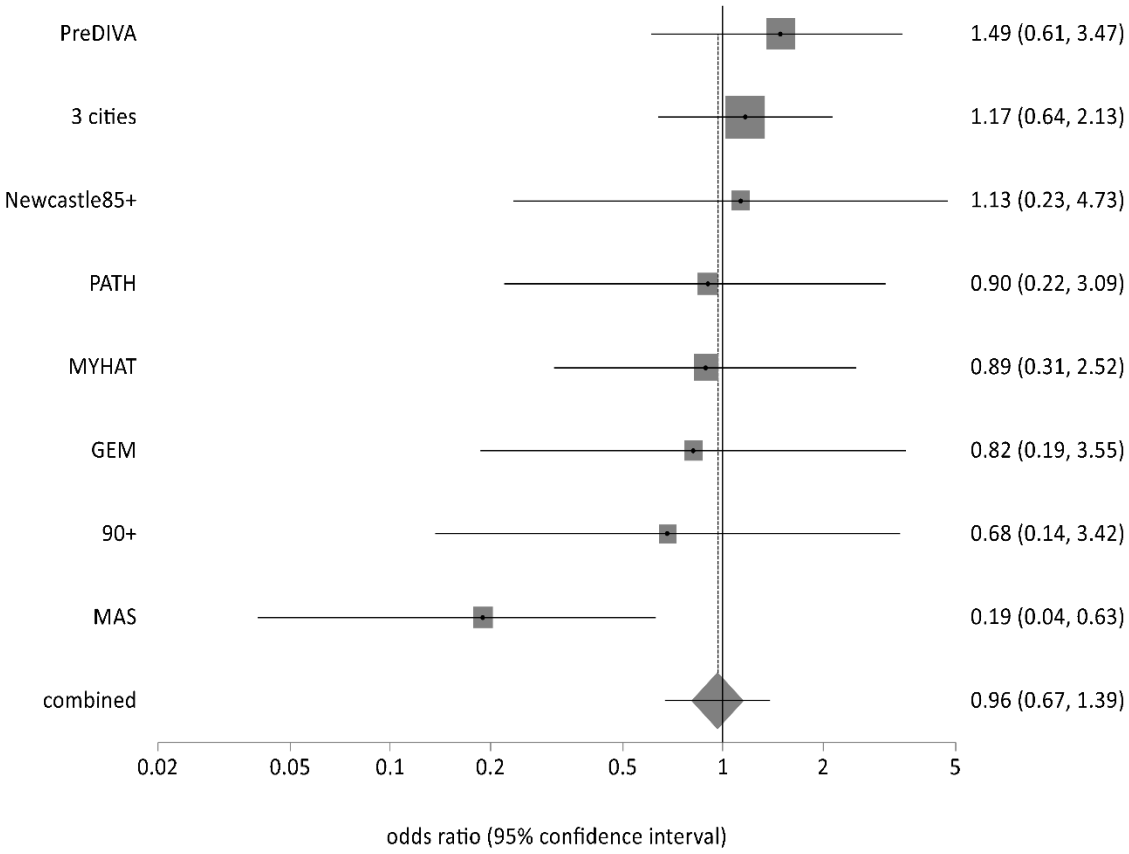
CCB, MMSE cognitive decline, ≥5 year



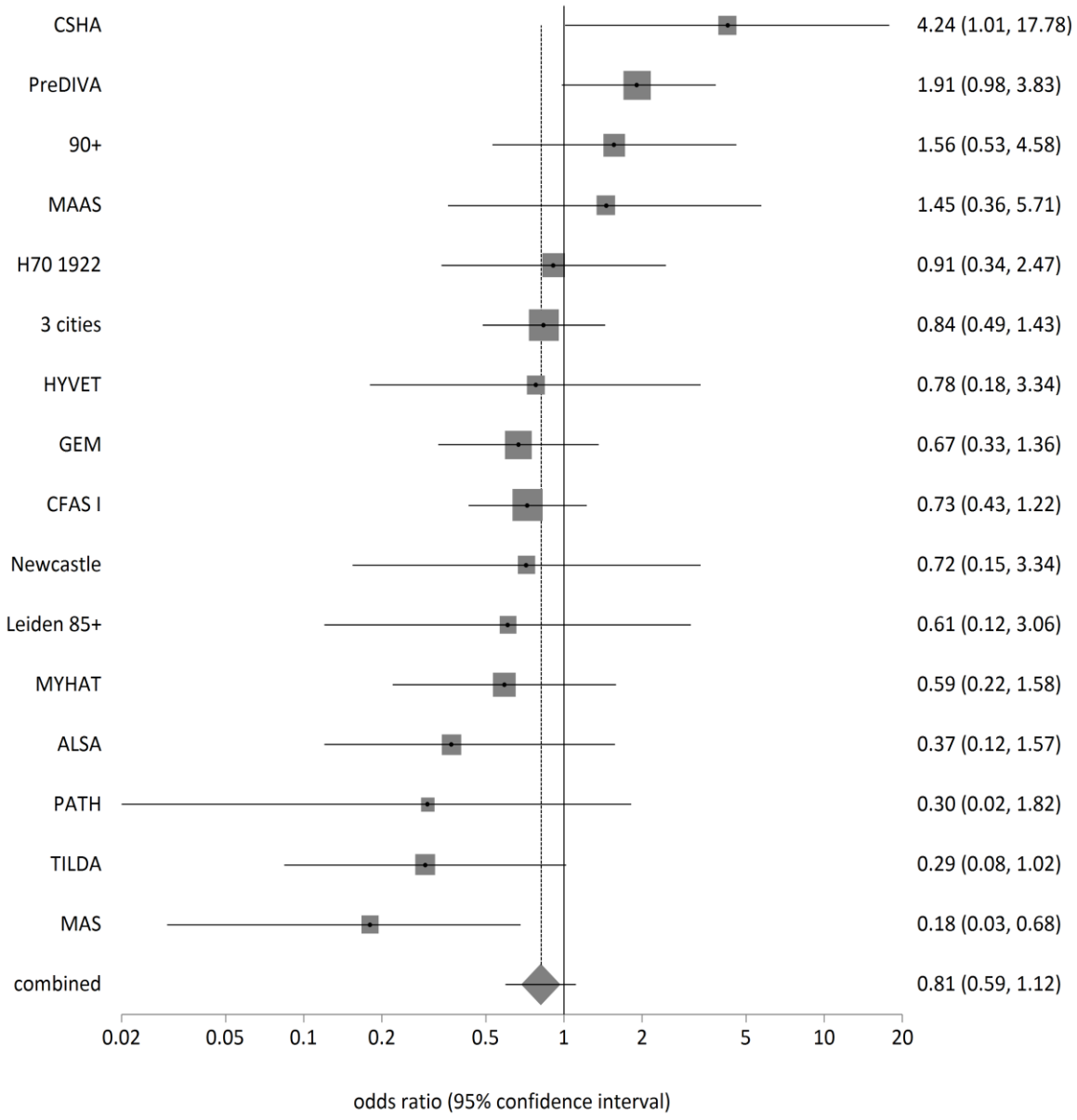
ACE-I, MMSE cognitive decline, ≥5 years



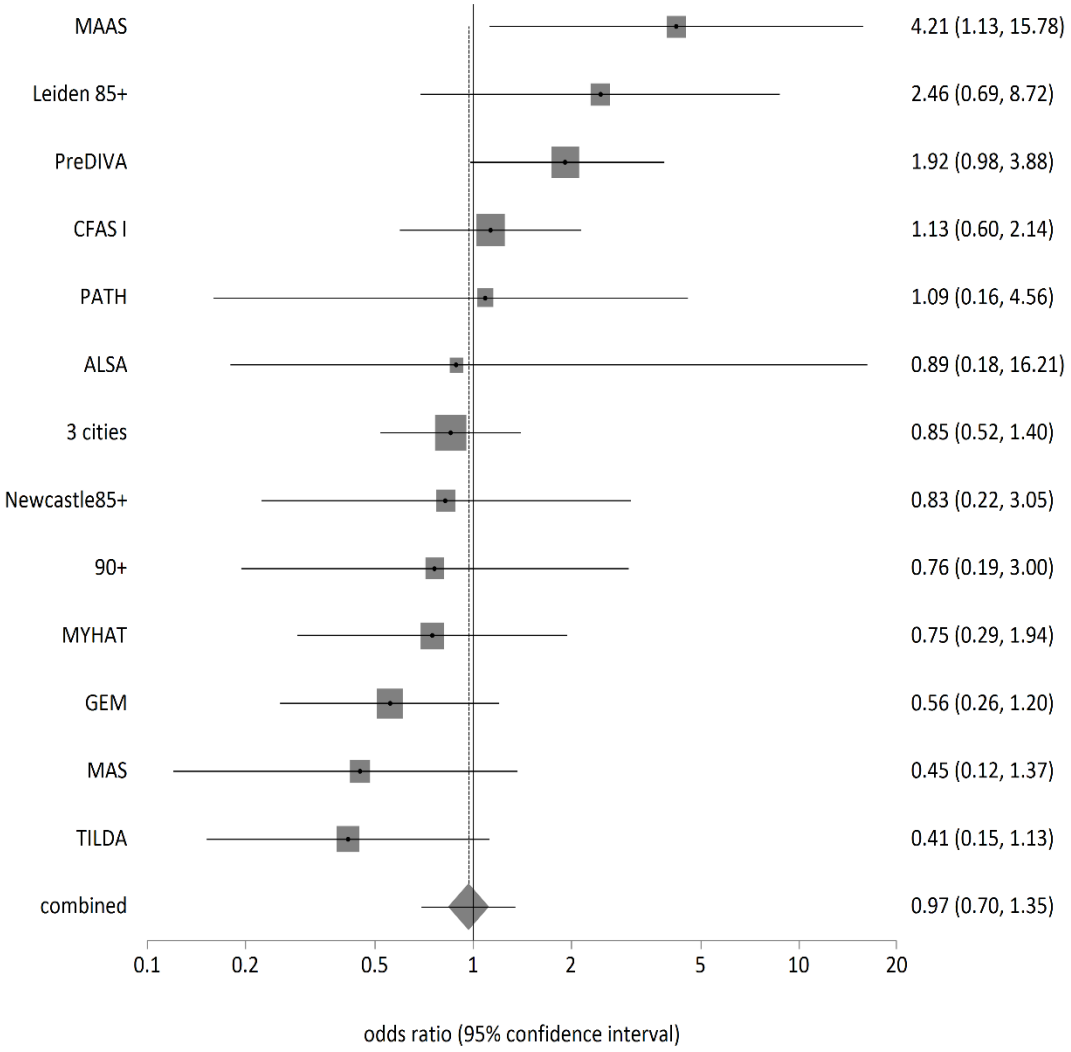
ARB, MMSE cognitive decline, ≥5 year



Diuretic, MMSE cognitive decline, ≥5 years



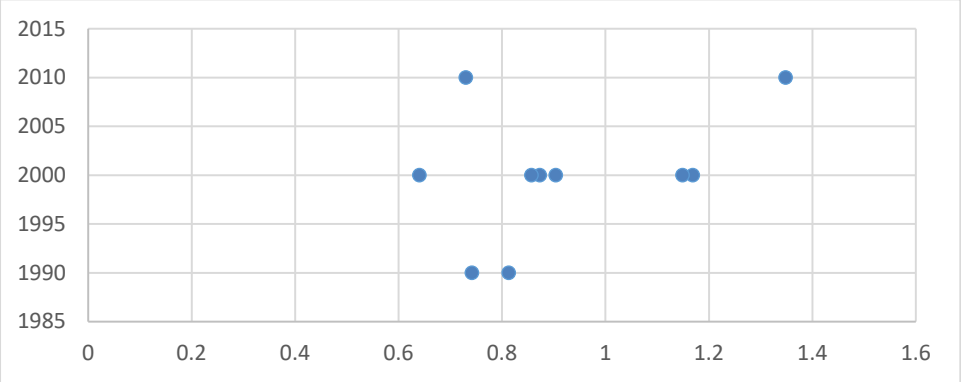
BB, MMSE cognitive decline, ≥5 years



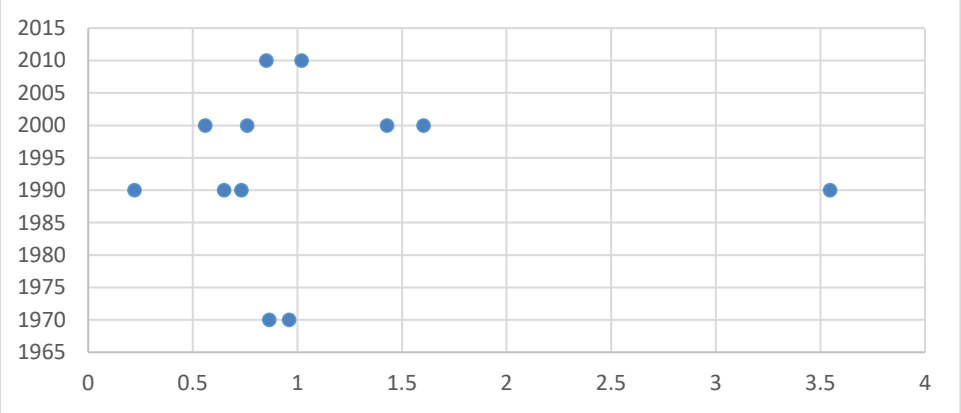
appendix C Comparison of study characteristics

Figures plotting study odds ratios for antihypertensive treatment compared to no treatment or placebo against primary decade of recruitment for those aged >65 years

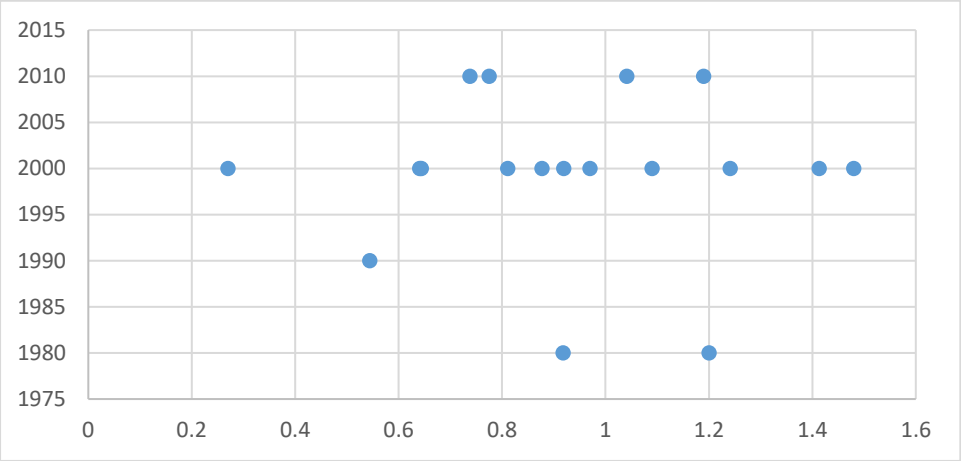
Dementia, those with ≥1 year follow-up



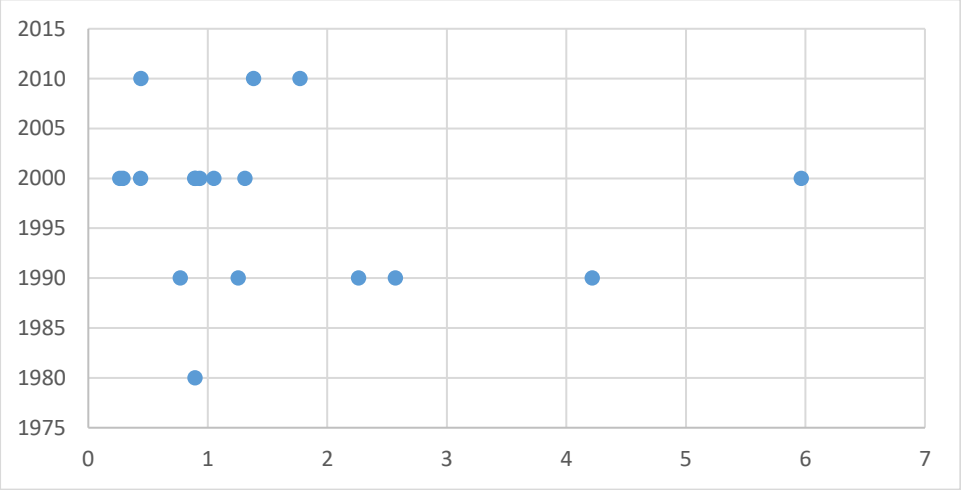
Dementia, those with ≥5 year follow-up



Cognitive decline (MMSE), those with ≥1 year follow-up

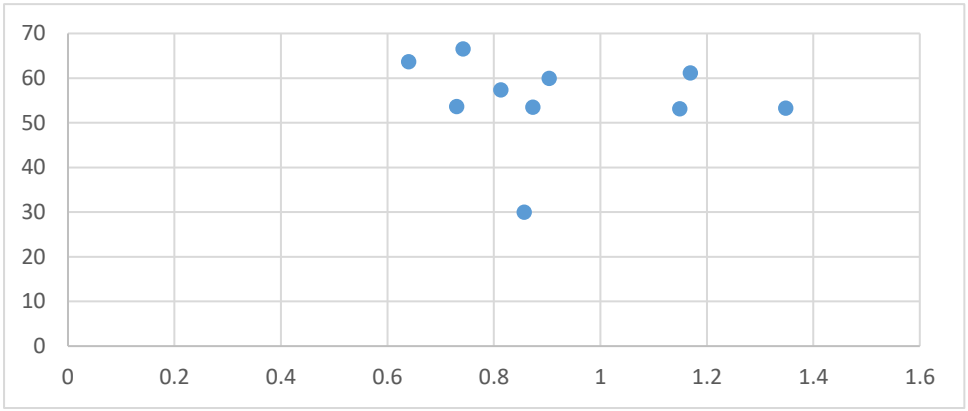


Cognitive decline (MMSE), those with ≥5 year follow-up



Figures plotting study odds ratios for antihypertensive treatment compared to no treatment or placebo against the percentage of study participants that were female, for those aged >65 years

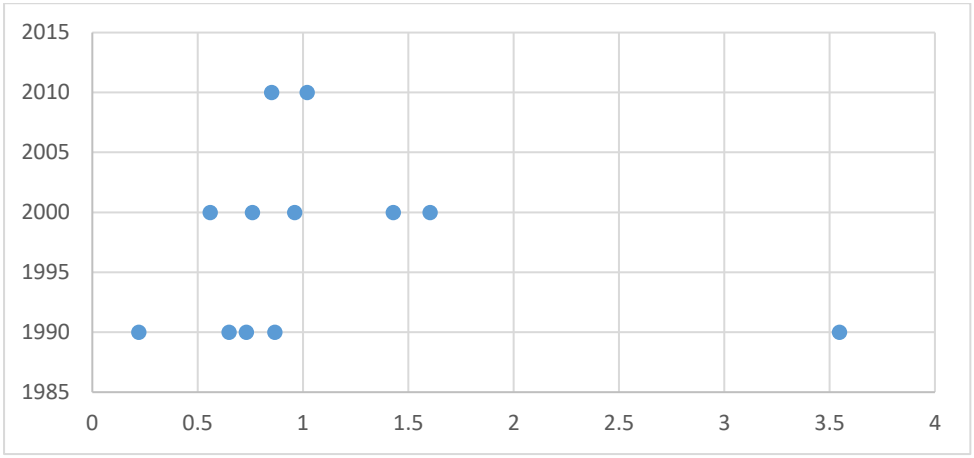
Dementia, those with ≥1 year follow-up



% female

Odds Ratio point estimate

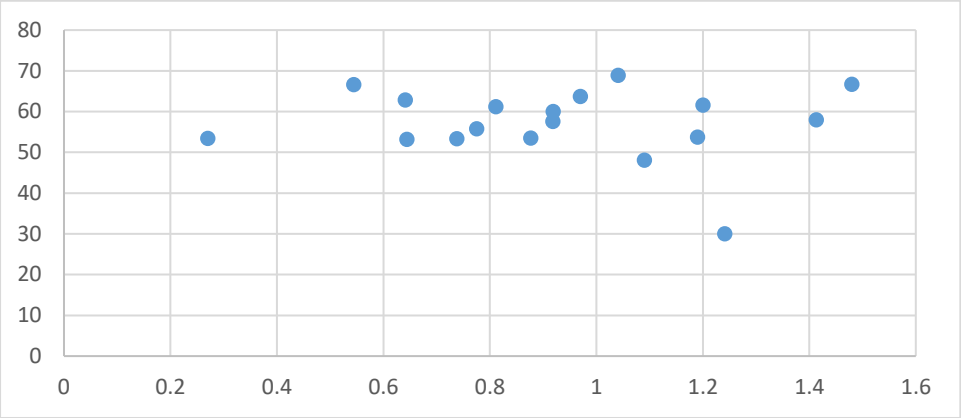
Dementia, those with ≥5 year follow-up



% female

Odds Ratio point estimate

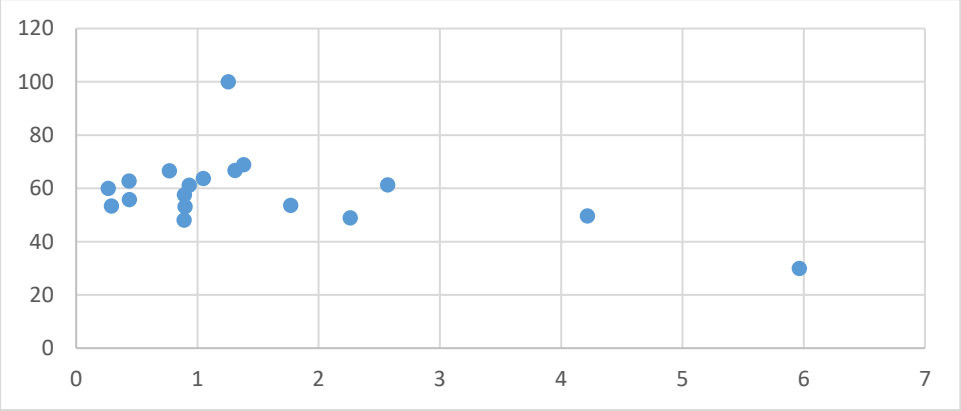
Cognitive decline (MMSE), those with ≥1 year follow-up



% female

Odds Ratio point estimate

Cognitive decline (MMSE), those with ≥5 year follow-up



% female

Odds Ratio point estimate